SUPPLEMENT 5

HONG KONG MEDICAL JOURNAL 香港醫學雜誌 30(S5)

Volume 30 Number 4 August 2024

HONG KONG MEDICAL JOURNAL
香港醫學雜誌

The official publication of the
Hong Kong Academy of Medicine and
the Hong Kong Medical Association

Health and Medical Research Fund
Research Dissemination Reports
醫療衞生研究基金
研究成果報告

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眼睛症狀

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Infection
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Chinese medicine
中醫藥

Volume 30 Number 4 August 2024

Supplement 5

ISSN 1024-2708

香港醫學專科學院出版社
HONG KONG ACADEMY OF MEDICINE PRESS

HONG KONG MEDICAL JOURNAL 香港醫學雜誌
Volume 30 Number 4 **August 2024**
SUPPLEMENT 5

Health and Medical Research Fund

Research Dissemination Reports

INFECTION

CHINESE MEDICINE

Editorial

Dissemination reports are concise informative reports of health-related research supported by the Health and Medical Research Fund administered by the Health Bureau. In this edition, we present 11 dissemination reports of projects related to cancer, children's health, eye disorder, health services research, primary care and preventive medicine, infection, and Chinese medicine. In particular, research findings of three projects may provide insights to enhance clinical practices and help inform health policy formulation in Hong Kong.

Caring for children with life-limiting diseases can be challenging for parents who are fully occupied managing their child's care, often resulting in fatigue and family tension. Communication between parents and healthcare providers is essential for ensuring continuity of care and discussing treatment options. Paediatric palliative care is recommended after a diagnosis of a life-limiting disease, but access to this service is limited. Wong et al[1] explored the perceived needs of paediatric patients with life-limiting diseases from the perspectives of affected children, parents, and healthcare providers. Needs were identified related mainly to understanding and living with the disease, and coordination and continuity of care. Greater parental engagement in care planning and management with healthcare professionals was suggested. Paediatric palliative care was recommended to be introduced after diagnosis of a life-limiting disease, and nurse case managers could facilitate continuity of care and interdisciplinary communication.

Glaucoma is the leading cause of blindness in Hong Kong. Primary open-angle glaucoma is a chronic disease that requires long-term treatments such as eye drops, laser, and surgery to reduce intraocular pressure. Management decisions are usually made by the clinician, but shared decision-making emphasising patient autonomy, informed consent, and patient empowerment is becoming more common. Choy et al[2] developed a patient decision aid (PDA) and conducted a single-centre randomised controlled trial among 160 Chinese patients with primary open-angle glaucoma to determine the effectiveness of PDA at improving decision making. The study findings showed that the PDA was effective at significantly improving patients' disease knowledge and self-confidence in medication adherence and resulted them having higher confidence in making decisions that suited their needs.

Hospital readmissions can be costly and are often associated with adverse outcomes. The 30-day readmission rate in Hong Kong is about 17%, of which over 40% could have been avoided. Chung et al[3] used systematic reviews and network meta-analyses with a Delphi consensus-building framework to develop unique peri-discharge nurse-led interventions that were aimed at reducing 30-day avoidable hospital readmissions for general medicine patients, patients with heart failure and chronic obstructive pulmonary disorders, and colorectal surgery patients. The recommended list of interventions could be used by healthcare policy-makers to guide resource allocation and inform the implementation and optimisation of interventions in the Hong Kong public healthcare system.

Supplement editors

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Epidemiology, prognosis, risk factors, and chemopreventive agents for post-colonoscopy colorectal cancer: abridged secondary publication

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KEY MESSAGES

1. In Hong Kong, post-colonoscopy colorectal cancer (PCCRC) is associated with higher prevalences of distal cancers (>80%) and cancer-specific mortality, compared with detected colorectal cancer. The rate of PCCRC at 3 years is 7.9%.
2. Predictive factors for PCCRC at 3 years are older age, male sex, history of colonic polyps, polypectomy/biopsy at index colonoscopy, index colonoscopy by a surgical endoscopist, and a higher centre annual colonoscopy volume.
3. Non-steroidal anti-inflammatory drugs have potential chemoprotective effects against PCCRC.
4. Statins are potential chemopreventive agents against PCCRC.

Hong Kong Med J 2024;30(Suppl 5):S4-6
HMRF project number: 16173001

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Introduction

Colorectal cancer (CRC) is the third most common cancer in men and the second most common cancer in women. In 2015, there were 1.65 million newly diagnosed cases of CRC and 835 000 CRC-related deaths. Colonoscopy screening is an effective means to reduce CRC incidence and mortality.[1] However, CRC can occur between colonoscopy screening procedures, a condition known as post-colonoscopy CRC (PCCRC).[2] The PCCRC rate is an indicator of colonoscopy service quality in CRC detection and prevention. Non-steroidal anti-inflammatory drugs (NSAIDs)[3] and statins[4] can decrease CRC risk, but no stratified analysis has been performed with a focus on interval PCCRC.

Methods

The Clinical Data Analysis and Reporting System was searched to retrieve relevant data from 2005 to 2016. The World Endoscopy Organization consensus was used to define the PCCRC rate at 3 years: CRC diagnosed between 6 and 36 months after a colonoscopy in which no CRC was detected. The definition of 'detected CRC' was CRC diagnosed within 6 months of the index colonoscopy, based on the assumption that CRC suspected at the index colonoscopy would be confirmed within this period.

Patients aged ≥40 years who underwent colonoscopy during 2005 to 2013 were identified. Patients with a history of CRC, inflammatory bowel disease, or previous colectomy were excluded. The CRC sites were categorised as distal colon (from rectum to splenic flexure) and proximal colon (from transverse colon to cecum).

Factors evaluated for associations with PCCRC development, relative to detected CRC, included patient characteristics, endoscopy centre polypectomy rate, and annual endoscopy volume. Endoscopy centre characteristics included the annual polypectomy rate (divided into four quartiles: <21.3%, 21.3%-24.0%, 24.1%-27.7%, >27.7%) and annual colonoscopy volume (divided into four quartiles: <2033, 2033-2923, 2924-3363, >3363). Patient characteristics included sex, age at index colonoscopy, presence of colonic polyps, biopsy/polypectomy at index colonoscopy, cigarette use, alcohol intake, and presence of comorbidities (obesity, hypertension, diabetes mellitus, dyslipidaemia, ischaemic heart disease, atrial fibrillation, stroke, congestive heart failure, chronic renal failure, cirrhosis, parkinsonism, and dementia). These comorbidities increase PCCRC risk due to inadequate bowel preparation. Survival was calculated from CRC diagnosis until death or the end of the study (31 December 2017).

Outcome measures included use of NSAIDs, statins, and aspirin prior to index colonoscopy. Patient factors, endoscopy centre performance, and concurrent medication use were considered in analyses of PCCRC risk at 3 years.

All drug prescription and dispensing data were

tracked up to 5 years before the index colonoscopy. Medication use was defined as ≥90 days of usage.

Results

Of 234 827 patients, 197 902 who underwent colonoscopies during the 9-year study period were included in the analysis. The rate of detected CRC was 5.1% (n=10 005), and the PCCRC rate at 3 years was 0.4% (n=854). Among patients with PCCRC at 3 years, 82.8% (n=707) and 17.2% (n=147) exhibited CRC in the distal colon and proximal colon, respectively. The overall incidence was 15.2 per 10 000 person-years. The overall PCCRC rate at 3 years was 7.9% for the period 2005 to 2013. The PCCRC rate at 3 years increased from 4.1% in 2005 to 9.7% in 2009 (Poisson P<0.001) and then decreased from 9.7% in 2009 to 7.7% in 2013 (Poisson P=0.046).

Compared with patients with detected CRC, patients with PCCRC at 3 years were older at index colonoscopy (74.6 vs 71.9 years, P<0.001) and at CRC diagnosis (75.9 vs 72.0 years, P<0.001). The median time from baseline to diagnosis of PCCRC was 1.2 (interquartile range, 0.8-1.9) years. Higher percentages of patients with PCCRC at 3 years had proximal involvement (17.2% vs 9.8%, P<0.001), a history of colonic polyps (35.8% vs 25.4%, P<0.001), and comorbidities including congestive heart failure and atrial fibrillation.

Multivariate analysis revealed that the diagnosis of PCCRC at 3 years was associated with older age (adjusted odds ratio [aOR]=1.07, 95% confidence interval [CI]=1.06-1.08), male sex (aOR=1.45, 95% CI=1.26-1.67), polypectomy/biopsy at index colonoscopy (aOR=3.97, 95% CI=3.46-4.56), a history of colonic polyps (aOR=1.31, 95% CI=1.13-1.51), index colonoscopy by a surgical endoscopist (aOR=1.53, 95% CI=1.31-1.78), and a higher annual centre colonoscopy volume (compared with quartile 1, aORs were 1.09 [95% CI=0.89-1.35] for quartile 2, 1.50 [95% CI=1.22-1.85] for quartile 3, and 1.83 [95% CI=1.50-2.24] for quartile 4).

Patients were followed up for up to 13 years; 6011 (55.4%) of all patients with CRC died, and 3413 (31.4%) of these deaths were cancer related. The 1-year, 3-year, 5-year, and 10-year cancer-specific survival probabilities were 83.2%, 70.6%, 66.1%, and 63.4%, respectively.

Cancer-specific survival was worse among patients with PCCRC at 3 years than among patients with detected CRC (log-rank P<0.001). The 1-year, 3-year, 5-year, and 10-year cancer-specific survival probabilities for PCCRC at 3 years were 74.3%, 60.8%, 57.7%, and 55.3%, respectively. The corresponding cancer-specific survival probabilities for detected CRC were 84.0%, 71.4%, 66.8%, and 64.0%, respectively.

Of 187 897 patients receiving NSAIDs, 91 961 (48.9%) were men. The follow-up duration was 560 471 person-years. In 5 years preceding the index colonoscopy, there were 21 757 NSAID users with a median use duration of 0.7 (interquartile range, 0.4-1.6) years. Among the NSAID users, 0.25% (n=55) were diagnosed with PCCRC at 3 years. The incidence rates for PCCRC at 3 years were 8.4 and 16.1 per 10 000 person-years among NSAID users and non-users, respectively.

Crude analysis showed that the hazard ratio (HR) for PCCRC at 3 years among NSAID users was 0.53 (95% CI=0.40-0.69) and the adjusted HR was 0.54 (95% CI=0.41-0.70). Stratified analysis indicated that NSAID use was associated with a reduced risk of PCCRC at 3 years in the proximal colon (adjusted HR=0.48, 95% CI=0.24-0.95) and distal colon (adjusted HR=0.55, 95% CI=0.40-0.74). The adjusted HR for PCCRC at 3 years among aspirin users was 1.01 (95% CI=0.80-1.28, P=0.92).

Statin users comprised 13.5% (n=25 447) of the cohort. The specific statins were simvastatin (69.7%, n=17 744), atorvastatin (7.3%, n=1847), and rosuvastatin (2.1%, n=542); 20.9% (n=5314) of patients switched between types. Among statin users, 0.5% (n=114) developed PCCRC at 3 years; the incidence rate was 15.0 per 10 000 person-years.

After propensity score matching, all covariates were balanced between statin users (n=17 662) and non-users (n=30 304) [absolute standardised difference <0.2]. Statin users had a decreased risk of PCCRC at 3 years (sub-distribution HR=0.72, 95% CI=0.55-0.95). Stratified analysis revealed that statin use was associated with a lower risk of PCCRC at 3 years in the proximal colon (sub-distribution HR=0.50, 95% CI=0.28-0.91) but not in the distal colon (sub-distribution HR=0.80, 95% CI=0.59-1.09).

Discussion

In Hong Kong, the PCCRC rate at 3 years was 7.9%, consistent with findings in Western populations that ranged from 0.8% of all colonoscopies to 9% of all diagnosed CRCs. The PCCRC rate at 3 years increased from 2005 to 2009 and then decreased from 2009 to 2013. The decrease may be related to the enhanced attention towards interval cancers, greater emphasis on adenoma detection, and adoption of high-definition endoscopes.

Patients with PCCRC at 3 years were older at cancer diagnosis, had a history of colonic polyps, and showed greater involvement of the proximal colon, compared with patients with detected CRC. Incomplete polypectomy was a risk factor for PCCRC development. A higher annual colonoscopy volume was associated with a greater risk of PCCRC at 3 years. Higher volume may result in a shorter procedure duration and thus a higher likelihood of missed lesions. However, we could not capture data regarding the duration of individual colonoscopy procedures.

Although proximal colon involvement was more prevalent in patients with PCCRC at 3 years than in patients with detected CRC, the distal colon was the predominant tumour site among patients with PCCRC at 3 years. This finding differs from previous findings, which indicated that proximal colon involvement was more common in PCCRC (50%-68%). The rate of PCCRC can exceed 15% among individuals with incomplete colonoscopy. In our latest colonoscopy registry, the rates of complete colonoscopy and caecal intubation are >95%. In 2017, distal CRC constituted 68.6% of all CRC cases. This percentage may explain the higher proportion of distal PCCRC at 3 years in the present study, considering that our centre predominantly serves Chinese patients, who reportedly have a higher prevalence of proximal cancer than distal cancer (56.5% vs 43.5%).

Patients with PCCRC at 3 years had a worse survival rate, compared with patients with detected CRC. This finding contrasts with a study conducted in Utah, which showed a better survival rate in patients with PCCRC. The discrepancy could be related to the earlier staging of PCCRC. Furthermore, the CRC site may play a role. The involvement of the proximal colon is commonly associated with aberrant methylation and microsatellite instability, implying distinct tumour biology associated with better survival, compared with microsatellite-stable CRC. Conversely, studies from Korea and Norway revealed no difference in cancer mortality between interval and detected CRC.

Regarding chemopreventive agents, NSAIDs were associated with a 47% reduction in the risk of PCCRC at 3 years in terms of both proximal and distal cancers. However, aspirin use did not show risk reduction. Cyclooxygenase-2 inhibition could play a crucial role in the chemopreventive effect of NSAIDs, but the inhibition is more selective in aspirin. Moreover, the chemopreventive effect of aspirin is evident only after >5 years of use with a latency period of at least 10 years, compared with a shorter period of time in NSAIDs. Statins demonstrated a dose-related chemopreventive effect on PCCRC at 3 years. Statins reduced the risk of PCCRC at 3 years by 28%, with a more pronounced effect on proximal CRC. Statins tend to act on later stages of the adenoma-carcinoma. Considering that pre-existing adenomas require approximately 10 years to progress to invasive cancer, we speculate that statins have the strongest effects on missed lesions (ie, those commonly located in the proximal colon) during the index colonoscopy, thereby impeding advanced adenoma progression to cancer.

Conclusion

In Hong Kong, the PCCRC rate at 3 years was 7.9%. Compared with Western populations, our cohort displayed lower cancer-specific survival and primarily distal colon involvement. NSAIDs and statins have potential chemopreventive effects on PCCRC development. Additional studies are needed to confirm our findings.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#16173001). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

Disclosure

The results of this research have been previously published in:

1. Cheung KS, Chen L, Seto WK, Leung WK. Epidemiology, characteristics, and survival of post-colonoscopy colorectal cancer in Asia: a population-based study. J Gastroenterol Hepatol 2019;34:1545-53.
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Acknowledgements

The authors thank research assistants Ms Lijia Chen, Ms Rachel Ooi, Ms Elaine Tan, and Mr Michael Lee for retrieving and organising data from the electronic healthcare database system for subsequent database compilation and data analysis.

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Needs of paediatric patients with life-limiting disease: abridged secondary publication

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KEY MESSAGES

1. Children with life-limiting diseases, their parents, and healthcare professionals all identified needs related to understanding the disease, living with the disease, and coordination and continuity of care.
2. There is a need for greater parental engagement in care planning and management, with support from healthcare professionals.
3. Paediatric palliative care facilitates holistic care for children with limited lifespans and should be introduced after the diagnosis is confirmed.
4. A nurse case manager on the paediatric palliative care team can facilitate continuity of care and interdisciplinary communication.

Hong Kong Med J 2024;30(Suppl 5):S7-10
HMRF project number: 16172581

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Introduction

Children with life-limiting diseases and their families face numerous challenges. Such children continue to grow and have developmental needs, along with healthcare and social needs. Caring for children with life-limiting diseases is a lifelong project for parents, who may experience fatigue because their time and space are fully engaged in managing the child's condition. Sometimes the spousal relationship is affected by the tension and disruption of normal family life.

Continuity of care is desirable, with coordination extending from hospital to home. Early and regular communication between parents and healthcare providers is essential for determining treatment options. Children with life-limiting diseases benefit from a palliative approach that advocates holistic care supported by an interdisciplinary team. The initiation of paediatric palliative care (PPC) is recommended after a diagnosis of life-limiting disease is confirmed.[1] The demand for PPC is increasing worldwide, but access to this service is limited. Currently, there are no data regarding the number of sick children requiring PPC in Hong Kong. The concept of palliative care is underdeveloped among paediatric patients, compared with adult patients. The Hospital Authority has established a strategic service framework for palliative care to support all patients with life-limiting conditions.

This study explored the perceived needs of paediatric patients with life-limiting diseases and opinions regarding PPC from the perspectives of affected children, parents, and healthcare providers.

Methods

Children aged 8 to 19 years with life-limiting diseases, as categorised by the Association for Children's Palliative Care Services,[1] who were not receiving active treatment, along with their families and healthcare providers, were recruited from five regional hospitals in Hong Kong between August 2019 and October 2021 for in-depth semi-structured interviews. All interviews were transcribed verbatim, and qualitative content analysis was independently performed by two researchers to explore similarities and variations in the perceived care needs of the three groups of participants. The agreement was 62.6% initially and reached 88.7% after repeated discussions until consensus.

Results

In total, 65 individuals (25 children, 25 parents, and 15 healthcare providers) in 25 cases were interviewed. Their mean ages were 13.5, 45.4, and 47.7 years, respectively. There were 44.0% female children, 68.0% mothers, and 46.7% female healthcare providers. According to the Association

for Children's Palliative Care Services, 8.0%, 24.0%, 28.0%, and 40.0% of the children's diseases were categorised as I, II, III, and IV, respectively (Table).

In total, 3784 units of needs of children with life-limiting diseases in three categories were analysed (Fig). Of these, 51.8% were from parents, 24.7% were from healthcare professionals, and 23.5% were from children. The category 'information and understanding about the disease' comprised 27.4% of the units in two subcategories: 'information and communication process' and 'understanding of child's condition and treatment process'. The category 'living with the disease' comprised 55.8% of the units in three subcategories: 'living with physical concerns', 'living with non-physical concerns', and 'perspectives of life'. The category 'care support and palliative care' comprised 16.8% of the units in two subcategories: 'continuity and coordination' and 'understanding of palliative care'.

In the category of 'information and understanding about the disease', doctors were identified as the primary source of information, although parents and children were able to search for information online. Patient groups were helpful in providing access to community resources. Healthcare professionals mainly provided medical information related to their own specialties; parents and children reported that this information was

TABLE. Characteristics of participants

	Children (n=25)*	Parents (n=25)*	Healthcare providers (n=15)*
Age, y	13.5±3.4	45.4±7.1	47.7±6.6
Sex			
Female	11 (44.0)	17 (68.0)	7 (46.7)
Male	14 (56.0)	8 (32.0)	8 (53.3)
Education			
Primary	9 (36.0)	2 (8.0)	-
Secondary	16 (64.0)	15 (60.0)	-
Tertiary or above	0	8 (32.0)	-
Association for Children's Palliative Care category			
I (curative treatment may be feasible but can fail)	2 (8.0)	-	-
II (long periods of intensive treatment needed to prolong life and allow normal activities)	6 (24.0)	-	-
III (progressive conditions without curative treatment options and treatment is exclusively palliative)	7 (28.0)	-	-
IV (irreversible but non-progressive, causing severe disability leading to health complications and premature death)	10 (40.0)	-	-
Marital status			
Single	-	0	-
Married	-	20 (80.0)	-
Widowed	-	3 (12.0)	-
Divorced	-	2 (8.0)	-
Employment			
Full-time	-	7 (28.0)	-
Part-time	-	3 (12.0)	-
None	-	15 (60.0)	-
Housing type			
Public	-	17 (68.0)	-
Private	-	8 (32.0)	-
Occupation			
Physician	-	-	13 (86.7)
Nurse	-	-	2 (15.3)
Experience in paediatric specialty, y	-	-	21.9±5.5 (7-31)

* Data are presented as mean±standard deviation, mean±standard deviation (range), or No. (%) of participants

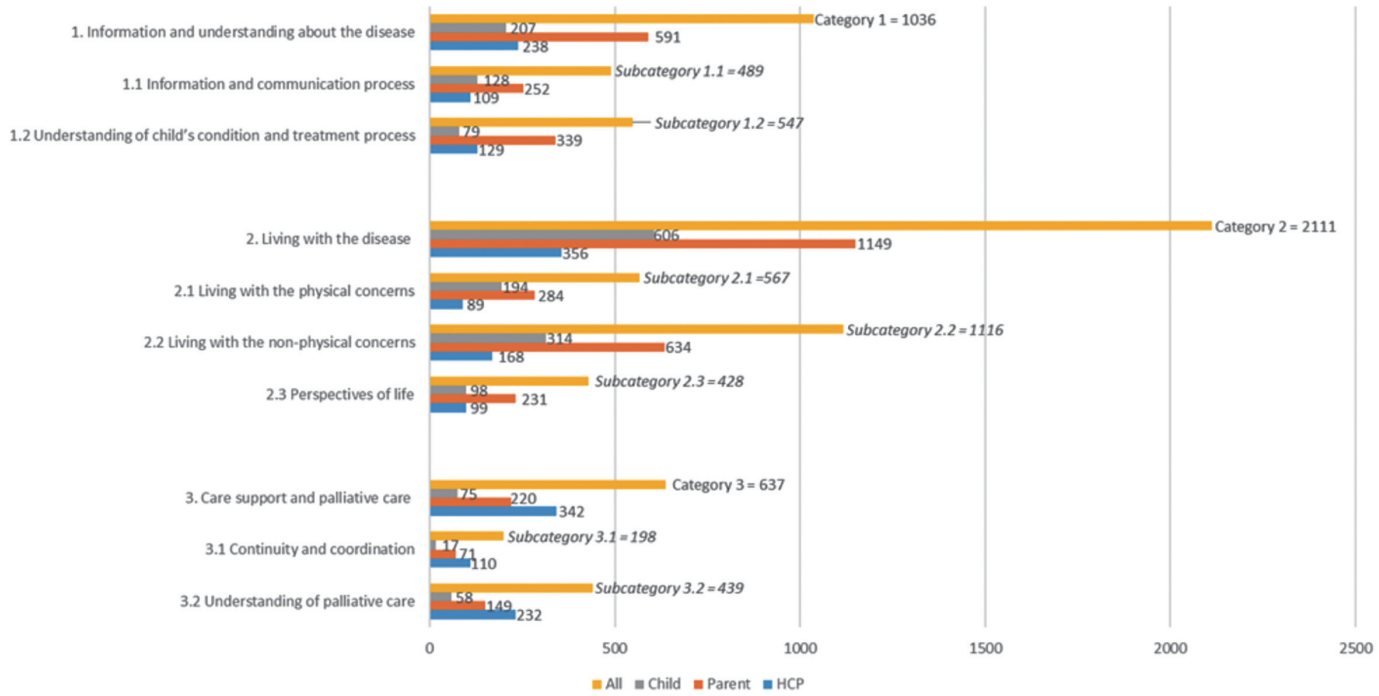

FIG. Needs of children with life-limiting diseases from the perspectives of affected children, parents, and healthcare professionals (HCP)

fragmented. Doctors acknowledged that they had minimal time available for patients and children during clinic consultations. Nurses often assumed the role of providing more detailed explanations; they acted as facilitators and agents of communication between patients/caregivers and doctors. The diagnosis stage could be a long process, followed by multiple treatments and repeated surgeries when the diagnosis was confirmed. In addition to Western medicine, alternative therapies were also regarded as care options.

The category of 'living with the disease' showed that children had both physical and non-physical concerns. Parents played a key role in supporting their children during daily living. Healthcare professionals supported parents in managing symptoms by arranging specialised equipment and teaching home-based nursing care. Caregivers, particularly mothers, had health issues themselves due to these heavy responsibilities. In some instances, spousal relationship was affected. Numerous emotional and psychological responses were identified in the subcategory 'living with non-physical concerns'. Parents and children both reported encountering social stigma. Children coped with psychosocial challenges by engaging in their favourite activities, with support from their parents. Although doctors noticed these psychosocial issues, they acknowledged lacking time to address such issues; nurses helped to fill this gap. In addition to hospital support, social and community support (ie, sponsorship for devices and activities) were also important. Children and their parents demonstrated realistic acceptance of the situation; children continued to plan their education and career.

The category of 'care support and palliative care' revealed concerns about continuity and coordination of care; healthcare professionals primarily focused on physical conditions. Healthcare professionals, children, and parents all noted that better coordination among specialties and better continuity of care were desirable. All three groups regarded palliative care as a more holistic approach to address their needs; they agreed that a nurse case manager could help coordinate interdisciplinary services and enhance continuity of care. Parents emphasised the need for early initiation of palliative care because of their children's limited lifespans, and healthcare professionals concurred.

Discussion

Children with life-limiting diseases and their parents experience complex challenges. There is an urgent need for better coordination and facilitation of care. Parents play an important role in caring for their children. Palliative care facilitates holistic care supported by a multidisciplinary team, thereby

optimising quality of life for both children and parents.

Children with life-limiting diseases go through several phases in their disease trajectory, from diagnosis to treatment, living with the disease with episodes of life-threatening events, and finally reaching the end-of-life phase.[2] Living with the disease involves functional limitations, constant interventions, and frequent surgeries that elicit fear and worry. Positive thinking, family support, and peer support are important, as are patient groups and community resources.

Parents often act as surrogate decision-makers, whereas children are passive recipients.[3] The parents in this study exhibited great resilience, but the demands on their well-being raised concerns. Changes in employment status and quality of life were reported by these parents. Such changes could lead to poor family functioning[2] and an increased caregiver burden. However, informal caregivers often are not engaged as key care planning partners in collaboration with healthcare professionals.[4] There is an urgent need to involve caregivers as essential members of the care team.[4]

The formation of a true partnership requires healthcare professionals to adapt to reciprocal information exchange and involve families as co-creators in care planning and coordination processes. Additionally, informal caregivers require training to enhance their knowledge and skills in home care provision and resilience, thereby protecting themselves from adverse effects on physical and mental health. Palliative care advocates holistic care and coordination and continuity of care supported by an interdisciplinary team.[1]

The palliative care approach aims to improve quality of life for individuals with life-threatening illnesses through early identification and management of problems in a holistic manner that involves coordinated multidisciplinary efforts. Engaging a key worker as a single point of contact to assist with care coordination is recommended. A narrative review suggested that nurses are the most appropriate individuals to assume such a role.[5] Participants who had experience with a nurse case manager confirmed that the service was beneficial. Early integration of PPC can support children with life-limiting diseases and their families in making sound and realistic decisions; symptom management can be enhanced by better care coordination. The Strategic Service Framework for palliative care, introduced to Hong Kong in 2017, has helped to promote PPC; however, the service remains underdeveloped. This framework guides the development of palliative care and services; it aims to support patients with life-limiting conditions by addressing their physical, psychological, and spiritual needs and improving their quality of life. Unlike adult palliative care services, PPC services are underdeveloped and carried out in an unstructured manner. Some hospitals do not have designated PPC teams. For example, two of the five study hospitals had a designated PPC team; the other hospitals provided PPC services in addition to their routine services.

Conclusion

This study highlighted the need for greater parental engagement in care planning and management for children with life-limiting diseases. Our findings can help inform healthcare policymakers and providers in the establishment of a PPC model.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#16172581). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

Disclosure

The results of this research have been previously published in:

1. Wong FKY, Ho, JMC, Lai TC, et al. Importance of parental involvement in paediatric palliative care in Hong Kong: qualitative case study. Arch Dis Child 2024;109:130-7.

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Timing of solid food introduction in Hong Kong children: abridged secondary publication

ASY Leung *, TF Leung, GWK Wong

KEY MESSAGES

1. The incidence of anaphylaxis has increased over the past decade. Hong Kong is experiencing a 'second wave of the allergy epidemic', particularly among young children.
2. Physician and public education and empowerment are needed to increase awareness of and preparedness for anaphylaxis.
3. Delayed introduction of allergenic solid foods is common in Hong Kong; further studies are needed to determine its role in the increasing anaphylaxis trend.

Hong Kong Med J 2024;30(Suppl 5):S11-3
HMRF project number: 04180047

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Introduction

The prevalence of food allergy (FA) has increased in the past decade; the highest challenge-confirmed FA prevalence was 10.4%, observed in Australian infants. FA impacts the health, quality of life, social interactions, and daily activities of affected individuals and their caregivers; it can also lead to severe allergic reactions and death. Thus, FA is an important public health problem. In Hong Kong, most healthcare professionals recommend that infants are introduced to solid foods at the age of 6 months, whereas some recommend delayed introduction of allergenic foods to high-risk infants. However, since the publication of the Learning Early about Peanut Allergy study,[1] early introduction of allergenic food to high-risk infants has been recommended. The disease burden of FA and food anaphylaxis in Hong Kong is unknown. We evaluated Hong Kong's disease burden of FA and food anaphylaxis, associated risk factors, and the associations between the timing of solid food introduction and FA in Hong Kong children.

Methods

Medical records of patients with anaphylaxis-related or allergy-related conditions (based on International Classification of Diseases (ICD) codes) who were admitted to Hong Kong's public hospitals between 2009 and 2019 were identified using the Clinical Management System. Data collected included details of allergic reactions, suspected allergens, age at onset, timing of solid food or food allergen introduction, test findings, and management plan (eg, prescription of adrenaline autoinjectors [AAIs]).

Additionally, patients with FA and/or anaphylaxis were prospectively recruited in seven major public hospitals in Hong Kong between June 2019 and December 2020. Patients and their caretakers were interviewed, and corresponding medical records reviewed. All patients with FA reactions underwent allergen-specific immunoglobulin E testing, including serological and skin prick tests.

Results

The 10-year incidence of anaphylaxis was 3.57 per 100 000 person-years. There was an increasing trend from 2009 to 2014 in both paediatric and adult populations, after which the incidence remained stable until 2019. The increase was more marked in the paediatric population than in the adult population; the respective incidence ratios in 2019 were 3.51 (95% confidence interval=1.12-2.66) and 1.82 (95% confidence interval=1.05-1.60). The incidence of new FA diagnosis increased from 2009 to 2019 (12.4 to 38.1 per 100 000 population), consistent with the increase in anaphylaxis incidence. Although the rate of AAI prescription increased for patients admitted with anaphylaxis, it remained below 15% and was lower in adult patients than in paediatric patients (36.5% vs 89.4%, P<0.001).[2]

Among paediatric patients with allergy-related symptoms (rather than those identified by ICD codes) who presented between 2010 and 2019,[3] the 10-year incidence of anaphylaxis was 9.76 per 100 000 person-years. The trend of anaphylaxis incidence increased over time. Food-induced anaphylaxis caused most hospital presentations; peanut and shellfish were the primary triggers. Most anaphylaxis episodes were classified as grade 4 severity, and young age was identified as a predictor for severe allergic reactions. Only 42.5% of cases were correctly coded as anaphylaxis using ICD-9 codes (995.0, 999.4, and 995.60 to 995.69); 29.7% of anaphylaxis episodes

were misclassified as angioedema (code 995.1). Adrenaline was administered in 42.2% of cases; 9.4% of these were administered prior to hospital arrival. Other predominant medications used for anaphylaxis were antihistamines (88.8%) and systemic steroids (51.6%). Four cases required intubation and three cases required cardiopulmonary resuscitation, but no deaths were reported. The use of adrenaline in hospitals increased during the study period but still lagged behind standard anaphylaxis management.

In collaboration with members of The Asia Pacific Academy of Pediatric Allergy, Respirology & Immunology, we initiated an Asian anaphylaxis registry using a standardised protocol. From June 2019 to December 2020, 100 episodes of anaphylaxis were recorded in Hong Kong. More than two-thirds of cases occurred in boys. The median patient age was lower in Hong Kong than in Singapore or Bangkok (1.14 [4.88-13.09] vs 4.95 [2.29-10.47] vs 10.67 [6.67-13.5] years). Most patients had no known history of anaphylaxis and presented with predominantly mucocutaneous features, followed by respiratory, gastrointestinal, cardiovascular, and neurological symptoms. Food was the predominant trigger in all three regions. Insect-induced anaphylaxis was only observed in Bangkok. Shellfish was the most common food allergen in Asia, followed by eggs, tree nuts, and peanuts. Most cases were under-recognised and undertreated; only 9% of patients were administered adrenaline prior to hospital arrival.

The timing of allergenic solid food introduction was analysed in 422 atopic cases and controls (Table). Of these, 32 (7.58%) were introduced to all seven common allergenic foods by 12 months of age; 17 (4.03%) had premature introduction of allergenic solid foods, including eggs and fish, before 4 months old. Delayed introduction (after 12 months of age) was common for tree nuts (77.0%, P<0.001) and peanuts (71.9%, P<0.001), whereas non-delayed introduction was common for fish (19.1%, P<0.001), eggs (17.4%, P<0.001), and cow's milk (14.0%, P<0.001) [Fig]. Despite the increasing evidence supporting non-delayed introduction of allergenic foods to prevent FA, delayed introduction (especially for nuts and peanuts), was common among Hong Kong children.

TABLE. Timing of allergenic solid food introduction in 422 atopic cases and controls

Allergenic solid food	Non-delayed introduction (≤12 months)*	Delayed introduction (>12 months)*	P value
Cow's milk	363 (86.0)	59 (14.0)	<0.001
Eggs	332 (82.6)	70 (17.4)	<0.001
Fish	326 (80.9)	77 (19.1)	<0.001
Shellfish	174 (44.2)	220 (55.8)	0.02
Wheat	170 (44.5)	212 (55.5)	0.03
Peanuts	108 (28.1)	276 (71.9)	<0.001
Tree nuts	87 (23.0)	292 (77.0)	<0.001

* Data are presented as No. (%) of participants

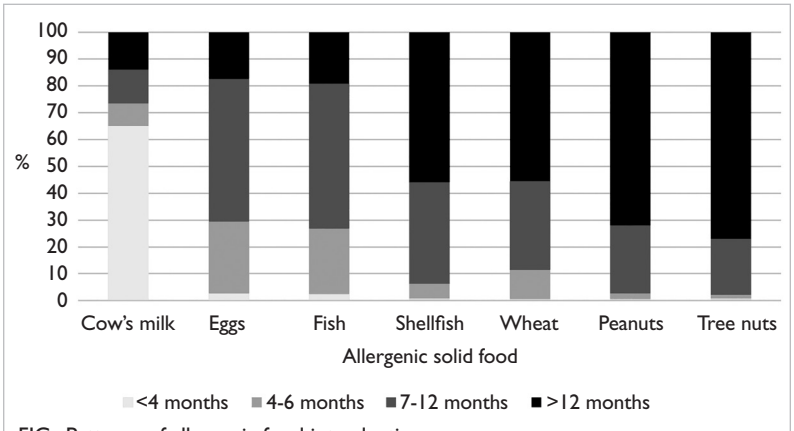

FIG. Patterns of allergenic food introduction

Discussion

The incidence of anaphylaxis between 2009 and 2014 is similar in Hong Kong and the West, but the rate of AAI prescription was lower in Hong Kong than in countries with similar disease burdens. Our findings highlight the need for physician and public education and empowerment to increase awareness of and preparedness for anaphylaxis. Delayed introduction of allergenic solid foods is common in Hong Kong; further studies are needed to determine its roles in the increasing anaphylaxis trend. The Hong Kong Anaphylaxis Consortium consensus statements are formulated to facilitate the prescription of AAIs by frontline physicians.[4]

A notable limitation of this study was the interruption of patient recruitment during the COVID-19 pandemic. Outpatient appointments for new cases were missed, and parents avoided hospital attendance. Nevertheless, most severe cases of allergic reactions were captured, but underestimation of the problem may persist.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#04180047). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

Disclosure

The results of this research have been previously published in:

1. Leung ASY, Li RMY, Au AWS, et al. Changing pattern of pediatric anaphylaxis in Hong Kong,

2010-2019. Pediatr Allergy Immunol 2022;33:e13685.
2. Tham EH, Leung ASY, Yamamoto-Hanada K, et al. A systematic review of quality and consistency of clinical practice guidelines on the primary prevention of food allergy and atopic dermatitis. World Allergy Organ J 2023;16:100770.
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Decision aids for patients with primary open-angle glaucoma: abridged secondary publication

BNK Choy *, MM Zhu, WWT Lam, JWH Shum

KEY MESSAGES

1. Decision aids can improve disease knowledge, increase patient confidence in medication adherence, and reduce decisional conflict among patients with primary open-angle glaucoma in Hong Kong.
2. Shared decision-making should be emphasised in the management of primary open-angle glaucoma because empowering patients to participate in their care can result in better decision-making outcomes.

Hong Kong Med J 2024;30(Suppl 5):S14-6
HMRF project number: 15161691

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Introduction

Glaucoma is the leading cause of blindness in Hong Kong, representing 23% of new registrations of permanent blindness in 2001-2002. The prevalence of primary open-angle glaucoma (POAG) in Asia is approximately 5%.[1] POAG is a chronic disease requiring long-term treatments that include eyedrops, laser, and surgery; all of which aim to reduce intraocular pressure.

Management decisions are usually made by clinicians. The choice of treatment primarily depends on clinicians' preferences, which may not be most appropriate for patients' needs. Shared decision-making emphasises patient autonomy, informed consent, and patient empowerment. Patient decision aids (PDAs) are tools designed to promote shared decision-making when multiple treatment options are available, each displaying benefits and harms that patients may value differently.[2] We developed a PDA in accordance with the International Patient Decision Aid Standards. We hypothesised that use of the PDA would be beneficial for patients with POAG.[3]

Methods

This was a single-centre randomised controlled trial. Consecutive patients were recruited from the outpatient glaucoma clinic at Lo Fong Shiu Po Eye Centre, Grantham Hospital. Eligible patients were randomly assigned to either the PDA group or the control group. Patients in the PDA group received a copy of the Chinese POAG PDA; they were briefly introduced its content and instructed to read the PDA at home.

The primary outcome measures included disease knowledge (measured by a 16-item disease knowledge questionnaire), patient self-confidence in overcoming barriers to medication adherence (measured by the 10-item Glaucoma Medication Adherence Self-Efficacy Scale [GMASS-10]), and decisional conflict (measured by the 16-item Decisional Conflict Scale [DCS]). Patients were evaluated face-to-face at baseline, 3 months, and 6 months.

Differences in outcome changes between the two groups were analysed using one-way analysis of covariance, with baseline fitted data as a covariate. Estimated mean group differences and corresponding 95% confidence intervals (CIs) were reported. The Holm-Bonferroni method was used to adjust the P values of DCS subscores between the PDA and control groups. A P value of <0.05 was considered statistically significant.

Results

At baseline, 160 patients aged 25 to 82 (mean, 59.3±9.5) years were recruited. At the end of the study, 156 patients remained: 77 in the control group (60 at 3 months and 73 at 6 months) and 79 in the PDA group (72 at 3 months and 77 at 6 months). The main reason for loss to follow-up was cancellation of clinic appointments during the COVID-19 pandemic. The two groups were comparable in terms of baseline demographic and clinical data (Table 1).

Disease knowledge scores were higher in the PDA group than in the control group at 3 months (12.0±2.3 vs 10.9±2.5) and 6 months (11.9±1.7 vs 11.1±2.6). After adjustment for baseline values, improvements in disease knowledge scores were significantly greater in the PDA group than in the control group at 3 months (1.15, 95% CI=0.5-1.8, F=12.6, P=0.001) and at 6 months (0.9, 95% CI=0.3-

TABLE 1. Baseline demographic and clinical data for all recruited patients

Demographic	Patient decision aid group (n=79)*	Control group (n=77)*	t or χ^2	P value
Age, y	59.5±9.4	59±9.9	-0.4	0.77
No. of women:men	36:43	32:45	0.1	0.71
Duration of glaucoma, y	7.9±7.2	7.2± 6.1	-0.51	0.61
Disease knowledge score	10.2±2.9	10.3±2.6	0.25	0.80
Glaucoma Medication Adherence Self-Efficacy Scale	22.8±6.5	22.3±7.0	-0.37	0.71
Decisional Conflict Scale	45.3±18.4	40.8±17.0	-1.6	0.11
Informed subscore	54.5±22.7	49.4±22.3	-1.7	0.5
Values clarity subscore	48.0±23.3	42.2±25.5	-1.7	0.5
Support subscore	38.3±20.3	33.8±18.2	-1.5	0.42
Uncertainty subscore	47.8±22.0	43.4±22.1	-1.4	0.36
Effective decision subscore	38.2±19.9	36.5±17.7	-0.7	0.54

* Data are presented as mean± standard deviation unless otherwise indicated

TABLE 2. Changes in scores of the Glaucoma Medication Adherence Self-Efficacy Scale and the Decisional Conflict Scale at 3 and 6 months

Scale	Mean change (95% confidence interval)		Mean group difference (95% confidence interval)	F	P value
	Patient decision aid group	Control group			
Glaucoma Medication Adherence Self-Efficacy Scale					
Change from baseline to 3 months	-1.6 (-2.7 to -0.5)	0.9 (-0.2 to 2.0)	-2.5 (-4.1 to -1.0)	10.1	0.02
Change from baseline to 6 months	-1.7 (-2.9 to -0.5)	0.2 (-1.0 to 1.5)	-1.9 (-3.7 to -0.2)	4.8	0.03
Decisional Conflict Scale					
Change from baseline to 3 months					
Total score	-13.9 (-16.8 to -11.0)	-5.1 (-8.0 to -2.1)	-8.8 (-12.9 to -4.6)	17.4	<0.001
Informed subscore	-20.3 (-24.0 to -16.6)	-8.9 (-12.6 to -5.1)	-11.4 (-16.7 to -6.1)	18.3	<0.001
Values clarity subscore	-18.5 (-22.3 to -14.7)	-9.2 (-13.1 to -5.4)	-9.3 (-14.7 to -3.9)	11.4	0.004
Support subscore	-10.0 (-13.3 to -6.7)	-2.6 (-6.0 to 0.7)	-7.4 (-12.1 to -2.7)	9.6	0.006
Uncertainty subscore	-12.8 (-16.6 to -9.0)	-5.1 (-9.0 to -1.2)	-7.7 (-13.2 to -2.2)	7.7	0.006
Effective decision subscore	-8.6 (-11.6 to -5.5)	-1.7 (-4.7 to 1.4)	-6.9 (-11.3 to -2.6)	9.8	0.004
Change from baseline to 6 months					
Total score	-18.3 (-21.4 to -15.2)	-4.6 (-7.8 to -1.3)	-13.5 (-18.0 to -8.9)	36.0	<0.001
Informed subscore	-26.4 (-30.4 to -22.5)	-8.4 (-12.5 to -4.4)	-18.0 (-23.7 to -12.3)	39.0	<0.001
Values clarity subscore	-23.2 (-27.5 to -18.9)	-5.7 (-10.0 to -1.4)	-17.5 (-23.6 to -11.5)	32.1	<0.001
Support subscore	-11.5 (-15.1 to -7.9)	-2.1 (-5.7 to 1.5)	-9.4 (-14.5 to -4.3)	13.5	<0.001
Uncertainty subscore	-18.9 (-22.6 to -15.2)	-5.8 (-9.5 to -2.0)	-13.1 (-18.4 to -7.8)	23.8	<0.001
Effective decision subscore	-12.5 (-15.9 to -9.2)	-3.4 (-6.8 to -0.01)	-9.1 (-13.9 to -4.4)	14.4	<0.001

1.5, F=9.8, P=0.02).

The GMASS-10 scores for self-confidence in medication adherence were lower in the PDA group than in the control group at 3 months (20.1±6.6 vs 23.3±6.1) and at 6 months (20.9±6.7 vs 22.6±7.0). After adjustment for baseline values, improvements in GMASS-10 scores were significantly greater in the PDA group than in the control group at 3 and 6 months (Table 2).

Total DCS scores for decisional conflict were

lower in the PDA group than in the control group at 3 months (30.2±13.9 vs 37.0 ±16.0) and at 6 months (25.6±13.3 vs 37.4±17.5). After adjustment for baseline values, reductions in DCS scores were significantly greater in the PDA group than in the control group at 3 and 6 months (Table 2).

Discussion

The PDA resulted in significant improvement in disease knowledge, but the small magnitude of this improvement may not be clinically significant. Therefore, we recommend additional patient education, especially regarding glaucoma treatments and outcomes, delivered through multiple formats (eg, lectures or videos) in addition to the PDA.

Improved medication adherence can lead to better disease outcomes and reduce drug wastage.[4,5] We observed significantly greater improvements in self-confidence in medication adherence (measured by the GMASS-10) in the PDA group than in the control group: 2.5 and 1.9 points better at 3 and 6 months, respectively. These results indicated that patients in the PDA group had greater self-confidence in adhering to their daily medication regimen.

The greatest improvement was observed in the DCS score. The PDA effectively helped patients to make confident decisions that best suited their needs. It enabled patients to make informed decisions while considering their own values. It is important for clinicians to empower patients with sufficient knowledge about their diseases and available treatment options to facilitate shared decision-making.

Conclusions

Our PDA can improve disease knowledge, increase patient confidence in medication adherence, and reduce decisional conflict among patients with POAG in Hong Kong. We recommend distributing the PDA to patients who may need to decide among different treatment options. The PDA can help patients to make an informed decision while considering their own values, rather than simply following clinicians' suggestions.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#15161691). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

Disclosure

The results of this research have been previously published in:

1. Zhu MM, Choy BNK, Lam WWT, Shum JWH. Randomized control trial of the impact of patient decision aid developed for Chinese primary open-angle glaucoma patients. Ophthalmic Res 2023;66:846-53.

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Role of microRNAs in sight-threatening diabetic retinopathy in Chinese patients: abridged secondary publication

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KEY MESSAGES

1. MicroRNA-related single nucleotide polymorphisms showed suggestive associations with sight-threatening diabetic retinopathy (STDR) in Chinese patients with type 2 diabetes.
2. MicroRNA profiling analysis identified several microRNAs that were differentially expressed between incident STDR cases and non-STDR controls.
3. Circulating microRNAs demonstrated the potential to serve as non-invasive biomarkers for prediction of STDR development.
4. Independent validation studies are required to confirm the findings of this study.

Hong Kong Med J 2024;30(Suppl 5):S17-20
HMRF project number: 06172266

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Introduction

Diabetic retinopathy (DR) is the most common microvascular complication of diabetes and can lead to vision loss. MicroRNAs (miRNAs) are a group of short, highly conserved, single-stranded, small, non-coding RNAs approximately 22 nucleotides in length. miRNAs post-transcriptionally modulate gene expression through mRNA degradation and the inhibition of protein translation via binding between the 3'-untranslated region of target mRNAs and the miRNA seed region. Dysregulated miRNA expression may play a role in the development of DR. Single nucleotide polymorphisms (SNPs) can alter miRNA function; SNPs involved in miRNA regulatory networks, such as those located in specific miRNA-encoding sequences or in miRNA-binding sites within the 3'-untranslated region of target genes, may have diverse functional consequences. These SNPs can alter miRNA expression, increase or decrease miRNA-target interactions, and create or disrupt miRNA-target interactions. This study aimed to (1) identify the miRNAs involved in sight-threatening (ST) DR by detecting STDR-associated miRNA-related genetic variants from a cross-sectional case-control genome-wide association study (GWAS) of STDR and a multiphase prospective nested case-control genome-wide circulating microRNA expression profiling analysis, and (2) evaluate the potential of the identified circulating miRNAs to serve as biomarkers for prediction of STDR development.

Methods

A cross-sectional case-control GWAS of STDR was conducted; 1000 STDR cases and 2195 non-STDR controls (mostly from the Hong Kong West Diabetes Registry cohort[1]) were included to identify miRNA-related variants that are associated with STDR. The grading of STDR was determined by ophthalmologists, based on the United Kingdom National Screening Committee classification.[2]

A multiphase prospective nested case-control genome-wide circulating miRNA expression profiling study, involving 124 incident STDR cases and 124 controls recruited from the same cohort,[1] was performed to identify novel circulating miRNAs that are related to STDR development. The potential for the identified circulating miRNAs to serve as non-invasive biomarkers for STDR prediction was then evaluated. The discovery phase included 24 incident STDR cases and 24 controls who remained free of STDR; they were matched in terms of age, sex, diabetes duration, haemoglobin A1c level, and hypertension status. Candidate miRNAs were then carried forward to the training phase for validation of the findings from next-generation sequencing. Significant miRNAs were then quantified by reverse transcription (RT)–quantitative polymerase chain reaction (qPCR) for the remaining 100 incident STDR cases and 100 controls for final validation.

STDR cases were defined as patients with type 2 diabetes mellitus who had either pre-proliferative DR (grade R2) or proliferative DR (grade R3). Non-

STDR controls were defined as patients without retinopathy or with background retinopathy (grade R1). Incident STDR cases were defined as patients who developed STDR between baseline assessment and 31 December 2017. Individuals who remained free of STDR through 31 December 2017 were regarded as controls in the miRNA profiling analysis.

For the detection of STDR-associated miRNA-related genetic variants, all participants were genotyped. Imputation was performed to maximise genetic coverage. miRNAs were extracted and used to generate the sequencing libraries, which were subsequently sequenced as paired-end reads of 151 base pairs. Candidate miRNAs were measured by RT-qPCR in the training and validation phases. A previously reported reference miRNA for DR, hsa-miR-328-3p, was used to normalise between-sample variation in RNA isolation.

The PLINK software was used for data management and manipulation. Stringent quality control was applied. In total, 7 645 048 polymorphic SNPs were examined to determine their associations with STDR in 943 STDR cases and 2072 non-STDR controls. A score-based test was used to examine the associations of SNPs with STDR; adjustment was made for age, sex, diabetes duration, haemoglobin A1c, hypertension status, and the first five principal components. Genome-wide significance was defined as $P<5 \times 10^{-8}$. The 'EBSeq' package in R software was used to identify differentially expressed miRNAs. To analyse the RT-qPCR results, the expression levels of miRNAs were normalised to the level of hsa-miR-328-3p. The Mann-Whitney *U* test was used to compare the expression levels of miRNAs in the matched case and control groups. Receiver operating characteristic curves and areas under the curve (AUCs) were used to evaluate the diagnostic utility of serum miRNAs.

Results

In total, 132 index SNPs showed suggestive associations with STDR after adjustment for covariates ($P<5\times10^{-5}$), although none achieved genome-wide significance. miRNA-related SNPs showing associations with STDR included *MIR2054-INTU* rs1344262 (odds ratio [OR]=1.36, 95% confidence interval [CI]=1.22-1.53, $P=9.13 \times10^{-8}$), CCBE1 rs1048008 (OR=0.77, 95% CI=0.68-0.87, $P=5.29 \times10^{-6}$), which was predicted to influence the binding of hsa-miR-183-5p, *AKAP13* rs117010213 (OR=2.63, 95% CI=1.70-4.07, $P=1.11 \times10^{-5}$), which may influence the binding of hsa-miR-1972; and *NMNAT1* rs10779735 (OR=0.75, 95% CI=0.65-0.86, $P=4.24 \times10^{-5}$), which was predicted to disrupt the binding site for hsa-miR-130b-5p and may create a binding site for hsa-miR-129-5p (Table 1).

In total, 2588 mature miRNAs were expressed in 48 serum samples. miRNAs were considered differentially expressed if their $\log_2$ fold change was ≥2 or ≤2 with false discovery rate–adjusted P<0.001. Eighteen miRNAs were upregulated in the incident STDR cases, including miR-183-5p. The expression levels of these 18 miRNAs were determined by RT-qPCR; 10 of them were significantly upregulated in the incident STDR case group (all P<0.05, false discovery rate–adjusted P<0.1, log2 fold change ≥2). These 10 miRNAs were then carried forward to the validation phase. All except hsa-miR-26b-5p were validated and displayed significant differences between the incident STDR cases and controls (all P<0.05, false discovery rate–adjusted P<0.05, Table 2).

Individual miRNAs only showed moderate AUCs ranging from 0.641 to 0.692 (Fig). The combination of all nine miRNAs showed a markedly increased AUC of 0.847 (95% CI=0.796-0.898). The AUC of a clinical model comprising risk factors

TABLE 1. Association results of microRNA-related genetic variants ($P<5 \times10^{-5}$)

Single nucleotide polymorphism	Nearest genes	Related microRNA	Odd ratios (95% confidence interval)	Adjusted P value	Functional relevance
rs1344262	*MIR2054-INTU*	hsa-miR-2054	1.36 (1.22-1.53)	9.13×10^{-8}	AKT3 was predicted to be a target of miR-2054. AKT regulates the expression of vascular endothelial growth factor, which plays a role in vascular dysfunction during diabetic retinopathy.
rs1048008	*CCBE1*	hsa-miR-183-5p	0.77 (0.68-0.87)	5.29×10^{-6}	Silencing miR-183 in mice with diabetic retinopathy inhibits tube formation and cell growth in the vascular endothelial cells by inhibiting the PI3K/Akt/vascular endothelial growth factor signalling pathway.
rs117010213	*AKAP13*	hsa-miR-1972	2.63 (1.70-4.07)	1.11×10^{-5}	miR-1972 promotes angiogenesis by targeting the p53/mechanistic target of rapamycin pathway.
rs10779735	*NMNAT1*	hsa-miR-130b-5p; hsa-miR-129-5p	0.75 (0.65-0.86)	4.24×10^{-5}	The expression of miR-130b is significantly upregulated in the vitreous humour of patients with proliferative vitreoretinopathy. Upregulation of hsa-miR-129-5p inhibits angiogenesis, cell migration, and invasion.

TABLE 2. Results of the validation phase of the microRNA profiling analysis

microRNA	Fold change	P value	False discovery rate–adjusted P value
hsa-miR-744-5p	1.28	4.38×10^{-6}	2.33×10^{-5}
hsa-miR-16-5p	1.77	4.65×10^{-6}	2.33×10^{-5}
hsa-miR-143-3p	1.65	8.56×10^{-6}	2.85×10^{-5}
hsa-miR-24-3p	1.31	1.15×10^{-5}	2.88×10^{-5}
hsa-let-7g-5p	1.31	3.29×10^{-5}	6.58×10^{-5}
hsa-miR-103a-3p	1.27	3.76×10^{-4}	6.27×10^{-4}
hsa-miR-126-5p	1.29	6.00×10^{-4}	8.57×10^{-4}
hsa-let-7d-5p	1.11	0.0187	0.023
hsa-miR-26a-5p	1.12	0.0434	0.048
hsa-miR-26b-5p	1.10	0.116	0.116

of haemoglobin A1c level, estimated glomerular filtration rate, body mass index, and hypertension was 0.560 (95% CI=0.480-0.640). When the nine miRNAs were included, the AUC significantly increased to 0.868 (95% CI=0.820-0.915, Fig).

Discussion

In the GWAS, the strongest association with STDR was exhibited by the intergenic variant rs1344262, located approximately 535 kb downstream of *MIR2054* and approximately 1.6 Mb distant from *INTU*. The 3'-untranslated region of AKT serine/threonine kinase 3 (AKT3) was predicted to be a target of miR-2054. AKT regulates the expression of vascular endothelial growth factor (VEGF), which plays an important role in vascular dysfunction during DR.[3] We detected suggestive associations of three genetic variants, which may affect various miRNA binding sites. However, none of these SNPs reached genome-wide significance.

Despite the relatively small sample size, we were able to identify substantially differentially expressed miRNAs. Some of these have demonstrated potential functional relevance to DR development. Several members of the let-7 miRNA family, such as hsa-let-7a-5p, reportedly are associated with DR. Due to their identical seed regions, all let-7 family members are suspected to possess similar functions. We demonstrated that the circulating levels of hsa-let-7d-5p and hsa-let-7g-5p were significantly elevated in patients with incident STDR. Hypoxia-inducible factor-1α upregulates let-7 and let-7-targeted argonaute 1, leading to reduced VEGF mRNA expression and angiogenesis.[4] Furthermore, let-7 family miRNAs were highly expressed in vascular cells, such as endothelial cells and vascular smooth muscle cells, suggesting

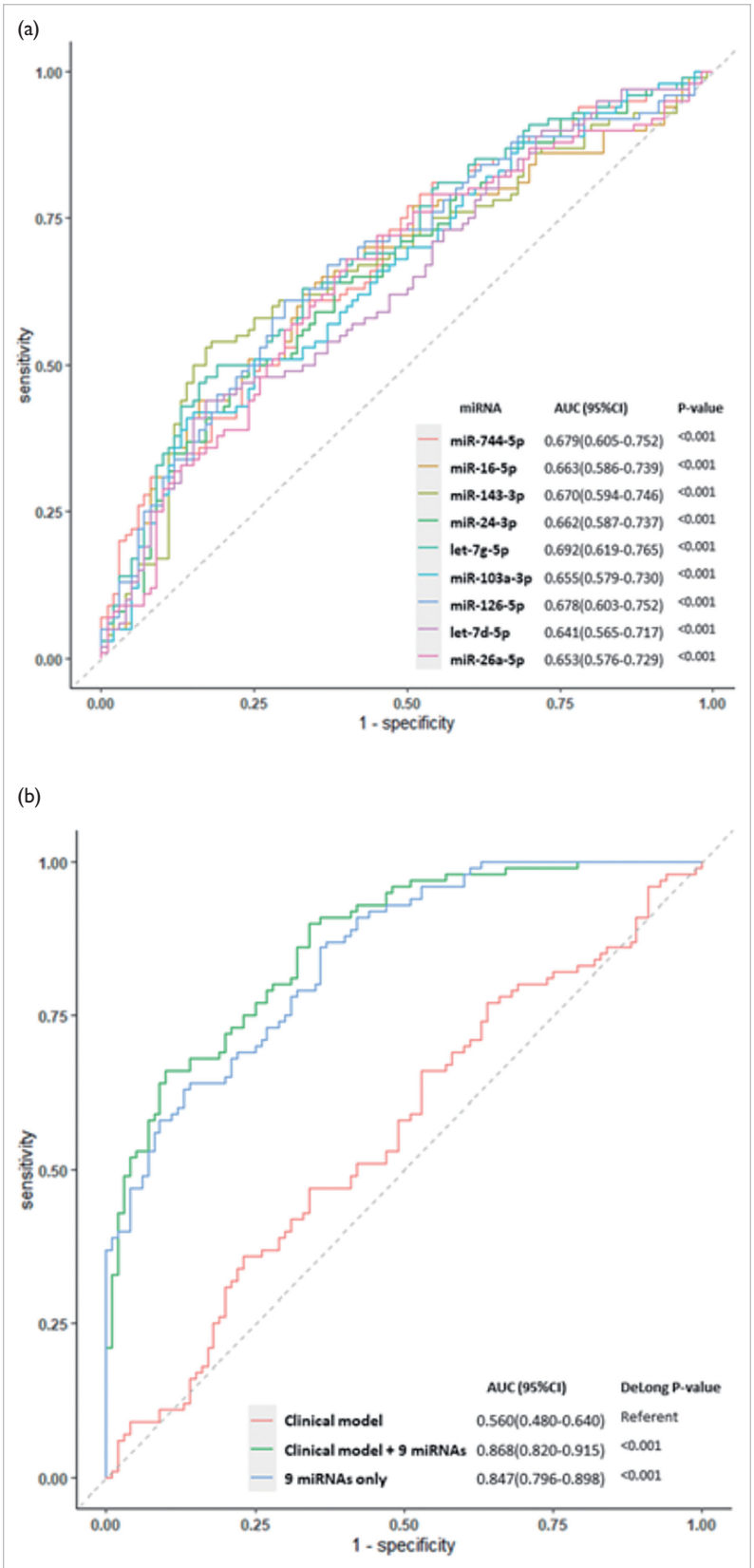

FIG. Receiver operating characteristic curve analysis for discrimination of incident sight-threatening diabetic retinopathy (STDR) cases and non-STDR controls: (a) the areas under the curve (AUCs) of all nine individual miRNAs range from 0.641 to 0.692, and (b) the AUCs of a clinical model (including risk factors of haemoglobin A1c level, estimated glomerular filtration rate, body mass index, and hypertension status), a model of nine miRNAs, and a combination of both; the AUC increases from 0.560 in the clinical model to 0.868 when the nine miRNAs are added.

that these miRNAs contribute to the regulation of vascular cell phenotypes. Patients with proliferative DR reportedly have elevated vitreous levels of hsa-miR-24-3p.[5] In the present study, serum hsa-miR-24-3p levels were increased in patients with incident STDR. VEGF and transforming growth factor β have roles in DR development. The predicted target genes for hsa-miR-24-3p were enriched in both VEGF and transforming growth factor β signalling pathways. Angiogenesis, a hallmark of DR development, was identified as an enriched subcategory in the GO enrichment analysis of predicted target genes of the identified miRNAs. Moreover, KEGG pathway enrichment analysis revealed that the predicted targets of these miRNAs were involved in the AGE-RAGE and MAPK signalling pathways, both closely related to DR development. These findings suggest that the identified miRNAs participate in STDR by regulating these pathways.

Although each individual miRNA only has moderate predictive value for STDR development (AUC=0.641-0.692), the combination of the nine miRNAs yielded a high AUC of 0.847. Furthermore, addition of the nine miRNAs to a clinical model significantly improved the AUC from 0.561 to 0.868, suggesting the potential for using these miRNAs as non-invasive biomarkers to predict STDR development.

Conclusion

Several potential miRNA-related SNPs are associated with STDR. We successfully validated a panel of miRNAs that are associated with incident STDR; they can serve as non-invasive biomarkers for predicting STDR development. Independent validation studies with larger sample sizes are warranted to validate our findings. Further functional analyses are required to elucidate the functional roles of the identified miRNAs in DR.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#06172266). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

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Peri-discharge nurse-led interventions for reducing 30-day hospital readmissions: abridged secondary publication

VCH Chung *, EK Yeoh, SYS Wong, CT Hung, HK Yip

KEY MESSAGES

1. Systematic reviews and network meta-analyses were used to synthesise peri-discharge nurse-led interventions for reducing 30-day hospital readmissions among patients with general medical conditions, heart failure, chronic obstructive pulmonary disease, or recent colorectal surgery.
2. Interventions adaptable to the Hong Kong public healthcare system and supported by local stakeholders were derived using the GRADE Evidence to Decision Framework.
3. The recommended list of interventions could be used by healthcare policymakers to guide resource allocation decisions and inform the implementation and optimisation of interventions in the Hong Kong public healthcare system.
4. Patients and caregivers are important stakeholders in healthcare delivery and intervention. Future research should involve patient and public participation efforts to co-create complex interventions and specific implementation strategies.

Hong Kong Med J 2024;30(Suppl 5):S21-4
HMRF project number: 16171031

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Introduction

Hospital readmissions are costly and associated with adverse outcomes. Many 30-day hospital readmissions can be prevented through appropriate peri-discharge interventions. Rates of 30-day hospital readmission are 20% in the United States and nearly 17% in Hong Kong. A systematic review of 34 studies showed that the median rate of preventable readmissions was 27% (range, 5% to 79%).[1] In Hong Kong, up to 40.8% of 30-day hospital readmissions were considered avoidable.[2] Efforts to reduce 30-day avoidable hospital readmissions can improve healthcare quality. We aimed to develop peri-discharge nurse-led interventions that could reduce 30-day avoidable hospital readmissions.

Methods

Peri-discharge nurse-led interventions were developed to reduce avoidable hospital readmissions among patients with general medical conditions, heart failure, chronic obstructive pulmonary disease (COPD), or recent colorectal surgery.

MEDLINE, EMBASE, Cochrane Database of Systematic Reviews, Global Health Database, and Allied and Complementary Medicine Database were searched, from inception to August 2019, for systematic reviews and randomised controlled trials related to peri-discharge nurse-led interventions for reducing preventable hospital readmissions.[3] Inclusion criteria for systematic reviews and randomised controlled trials are listed in Table 1. Intervention components were classified using an established coding framework. Pairwise meta-analysis was carried out using a random-effects model. Dichotomous data were presented as pooled risk ratios with 95% confidence intervals, whereas continuous data were presented as weighted mean differences with 95% confidence intervals. Network meta-analysis was then used to determine the most effective intervention for reducing 30-day all-cause hospital readmissions.[4]

To ensure that the selected peri-discharge nurse-led interventions were appropriate for the Hong Kong public healthcare system, a Delphi consensus based on the GRADE Evidence to Decision (EtD) framework[5] was independently conducted for each of the four conditions (general medical conditions, heart failure, COPD, and recent colorectal surgery). The Figure shows the step-by-step workflow for the Delphi consensus.

Eligible participants were frontline healthcare professionals from accident and emergency departments, convalescent hospitals, community geriatric assessment teams, university academics, and departments of general medicine, cardiology, respiratory, and surgery. Convalescent hospitals and community geriatric assessment teams were

TABLE 1. Inclusion criteria for systematic reviews and randomised controlled trials

Inclusion criteria	Systematic reviews	Randomised controlled trials
Participants	Patients aged ≥18 years admitted to an inpatient ward for ≥24 hours with a diagnosis of general medical conditions, heart failure, chronic obstructive pulmonary disease, or recent colorectal surgery. Patients with behavioural health issues or paediatric or obstetric admission were excluded.	
Interventions	Any pre-emptive peri-discharge interventions to reduce readmissions	
Comparisons	Any types of control including usual care	
Outcomes	Readmission outcomes in both intervention and control groups	30-day all-cause hospital readmissions in both intervention and control groups

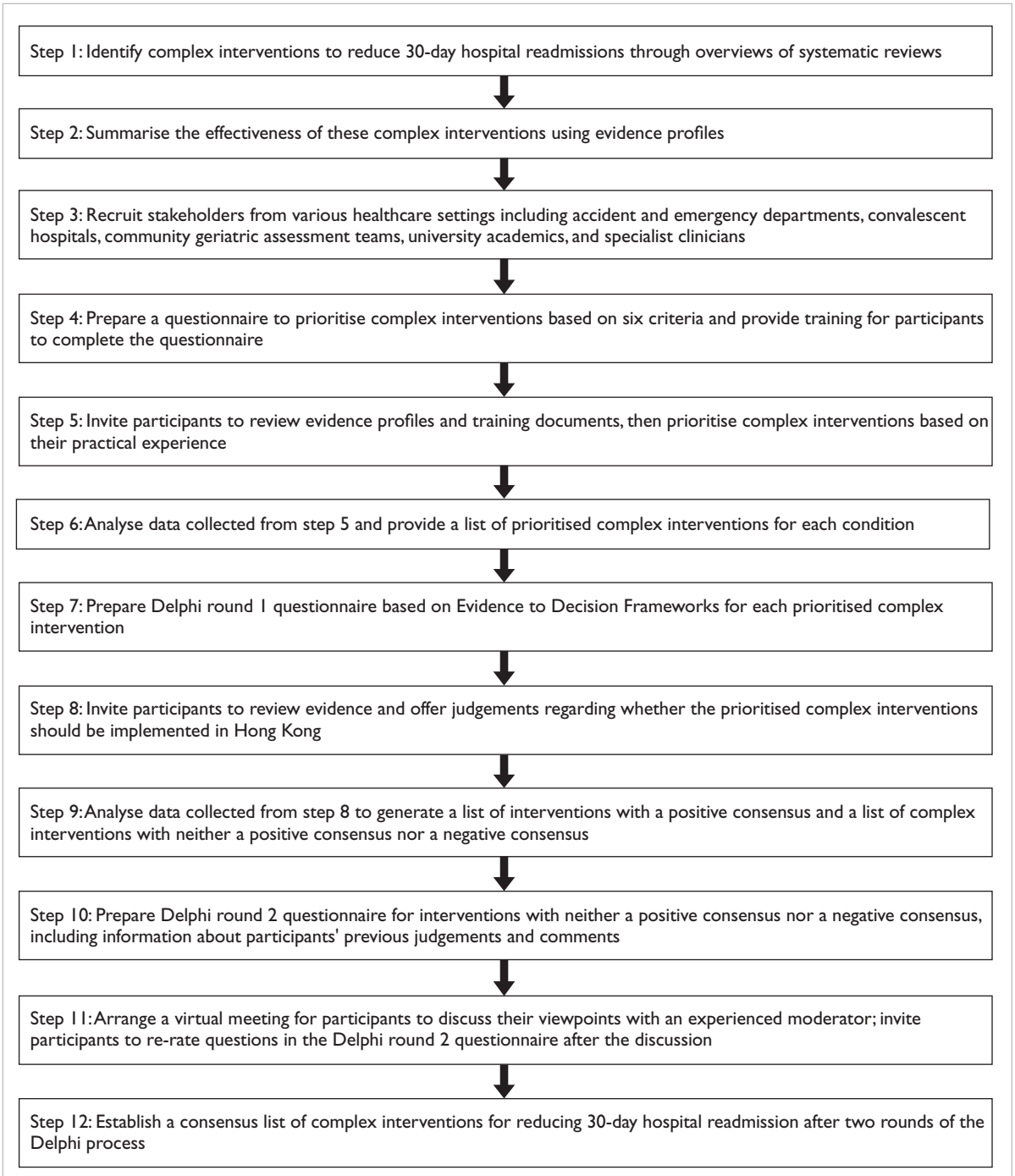

FIG. Workflow for adapting complex interventions for reducing 30-day hospital readmissions in the Hong Kong public healthcare system. This workflow was conducted separately for each condition. Experts from convalescent hospitals and community geriatric assessment teams were not involved in the panel for recent colorectal surgery.

not involved in the care for patients with recent colorectal surgery in Hong Kong; therefore, they were not involved in the corresponding panels. Stakeholders included chiefs of service, consultants, and team heads of the specific departments. Each panel comprised 18 participants, except for the recent colorectal surgery panel (n=10).

Participants were asked to determine whether the interventions should be prioritised using a Likert scale of 1 (least important) to 5 (most important). An intervention was prioritised if the summative rating score was ≥50% of the overall score (ie, a sum of all participants' ratings ≥45). New combinations suggested by ≥3 participants were also prioritised for further evaluation.

A two-round Delphi questionnaire was then produced for the prioritised interventions for the four conditions, based on the GRADE EtD framework, with respect to benefits, harms, values and preferences, equity, acceptability, and feasibility. Only interventions with neither a positive consensus nor a negative consensus were re-assessed. A virtual meeting was held to discuss the participants' judgements. The consensus cutoff level was 70%. A positive consensus was defined as ≥70% of participants rating to suggest/recommend an option, whereas a negative consensus was defined as ≥70% of participants rating to not suggest/recommend an option. A list of finalised interventions was developed for each condition, including all interventions with a positive consensus after two rounds.

Results

For general medical conditions, four nurse-led interventions were recommended to reduce 30-day hospital readmissions in Hong Kong (Table 2).

For heart failure, the supportive-educative intervention was considered the best intervention for reducing 30-day all-cause hospital readmissions, followed by the disease management intervention, which was considered the best intervention for reducing 30-day heart failure–related hospital readmissions. Five of 10 complex interventions for heart failure had a positive consensus; the percentage of agreement ranged from 72.2% to 83.3% (Table 2).

For COPD, complex interventions involving patient education, self-management, patient-centred

TABLE 2. Peri-discharge nurse-led interventions for patients with general medical conditions, heart failure, chronic obstructive pulmonary disease, or recent colorectal surgery.

General medicine conditions	Heart failure	Chronic obstructive pulmonary disease	Recent colorectal surgery
Intervention 1: components of primary care provider communication, provider continuity, case management, and streamlining	**Intervention A:** components of medication intervention and patient education	**Intervention I:** components of patient education, patient-centred discharge instructions, telephone follow-up, and case management	**Intervention a:** components of patient-centred discharge instructions and self-management
Intervention 2: components of primary care provider communication, provider continuity, discharge planning, and rehabilitation intervention	**Intervention B:** components of medication intervention, patient education, and self-management	**Intervention II:** components of patient education, patient-centred discharge instructions, telephone follow-up, and self-management	**Intervention b:** components of patient-centred discharge instructions, self-management, and rehabilitation intervention
Intervention 4: components of discharge planning and streamlining	**Intervention C:** components of medication intervention, patient education, self-management, telephone follow-up, community service, and scheduled follow-up	**Intervention IV:** components of provider continuity, rehabilitation intervention, discharge planning, and self-management	**Intervention c:** components of patient-centred discharge instructions, self-management, case management, and patient education
Intervention 5: components of case management, patient hotline, and telephone follow-up	**Intervention D:** components of medication intervention, patient education, self-management, telephone follow-up, case management, and discharge planning	Intervention VII: components of patient education and rehabilitation intervention	**Intervention d:** components of provider continuity, patient education, telephone follow-up, and case management
	Intervention E: components of telephone follow-up and patient hotline	**Intervention IX:** components of provider continuity, rehabilitation intervention, discharge planning, self-management, and patient education	**Intervention f:** components of self-management and telephone follow-up
	-	**Intervention X:** components of patient education, patient-centred discharge instructions, telephone follow-up, case management, provider continuity, rehabilitation intervention, discharge planning, and self-management	

discharge instructions, and telephone follow-up were significantly more effective than usual care in reducing 30-day hospital readmissions. Six complex interventions for COPD had a positive consensus; the percentage of agreement ranged from 70.6% to 94.1% (Table 2).

For recent colorectal surgery, network meta-analysis indicated no significant difference in reducing 30-day hospital readmissions across all complex interventions. However, fast-track rehabilitation was considered the most effective intervention for reducing the length of stay. Five of 12 complex interventions for recent colorectal surgery had a positive consensus; the percentage of agreement ranged from 75.0% to 88.9% (Table 2).

Discussion

The use of the GRADE EtD framework facilitated transparent recording of stakeholders' decisions and considerations while reaching a consensus. This transparency allows policymakers to assess the decision-making process, thereby enhancing the acceptability and creditability of the recommended interventions.

Conclusion

We identified peri-discharge nurse-led interventions for reducing 30-day hospital readmissions that could be adapted for the Hong Kong public healthcare system. Guided by the GRADE EtD framework, we developed a list of stakeholder-endorsed interventions for patients with general medical conditions, heart failure, COPD, or recent colorectal surgery.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#16171031). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

Disclosure

The results of this research have been previously published in:

1. Wong CH, Cheung WK, Zhong C, et al. Effectiveness of nurse-led peri-discharge interventions for reducing 30-day hospital readmissions: network meta-analysis. Int J Nurs Stud 2021;117:103904.
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Brain vitality enhancement for people with mild cognitive impairment in Hong Kong: abridged secondary publication

PWC Li *, DSF Yu, PM Siu, SCK Wong

KEY MESSAGES

1. A peer-supported exercise programme was developed to promote brain health among people with mild cognitive impairment.
2. The programme effectively sustained improvements in executive function, attention, and working memory among people with mild cognitive impairment.
3. The programme is highly feasible and acceptable for peer mentors and people with suboptimal cognitive function.
4. The high numbers of app downloads and content views indicate a strong need for education regarding mild cognitive impairment and strategies to prevent cognitive decline.

Hong Kong Med J 2024;30(Suppl 5):S25-9
HMRF project number: 01170728

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Introduction

People with mild cognitive impairment (MCI) are at risk of progression to dementia. Maintaining physical activity is a key strategy for preventing cognitive decline. Peer mentors are effective in enhancing older adults' engagement in physical activity. We developed a peer-support exercise programme—Brain Vitality Enhancement (BRAVE)—to promote brain health among adults with MCI. We examined the effects of the programme on cognitive function and physical and mental well-being among community-dwelling adults with MCI, along with participant satisfaction and programme acceptability.

Methods

The BRAVE programme consisted of two phases: (1) an empowerment workshop for peer mentors and (2) a supervised exercise programme for adults with suboptimal cognitive function.

Peer mentors who were both cognitively normal and physically active were recruited to attend an empowerment workshop that provides education about MCI, communication strategies for interacting with people with MCI, barriers to exercise and their solutions, and exercise safety. A mobile app was introduced to the peer mentors; the app was designed to promote self-directed learning, activity scheduling and tracking, and social networking between and/or within mentor-mentee groups. The peer mentors were trained in a structured exercise training module (three sessions/week for 3 weeks) about techniques for assisting with exercise setup, exercise demonstration, monitoring participants' execution, and motivating participants during the exercise. The workshop concluded with a booster session to consolidate the exercise and mentoring skills of peer mentors; their competency was evaluated via return demonstration.

People aged ≥50 years with MCI, who scored 19 to 26 on the Montreal Cognitive Assessment, were randomly assigned to receive either the BRAVE programme or usual care. Usual care comprised social and leisure activities that did not involve any structured exercise or cognitive training activities. Participants in the usual care group were later invited to join the BRAVE programme after completing the data collection. Participants in the BRAVE programme (8 to 10 per group) received three 60-minute exercise sessions per week for 8 weeks, delivered by a coach with the support of two to three peer mentors per group. The exercises simulated daily functional tasks. After the exercise module, a counselling session was conducted to help integrate the mentor-directed exercise training into the participants' lifestyles. The coach offered continuous support to the mentor-mentee groups through the app and visits during mentor-directed exercise sessions.

Outcome measures included the Alzheimer's Disease Assessment Scale–Cognitive subscale for global cognition, the digit span forward and backward tests for short-term and working memory, the Color Trails Tests 1 and 2 for executive function, and the Short Form 36 for health-related quality of life (HRQoL). Focus group interviews were

conducted to evaluate participant satisfaction and programme acceptability.

Results

Of 50 peer mentors recruited, 46 (mean age, 66.6 years) completed the training. They had good HRQoL at baseline. Their Short Form 36 physical and mental component scores did not significantly change before and after the training.

Of 250 people with MCI, 229 (mean age, 74.4 years) were included in the analysis; 85.6% of them were women. The overall adherence rate for the BRAVE programme was 81.0%; 92% of participants attended at least 75% of the sessions. Compared with the control group, the BRAVE group showed greater improvements in working memory, processing speed and attention immediately post-intervention and at 3 months, as well as sequencing and mental flexibility at 3 months (Fig). There were no significant between-group differences in short-term memory, global cognition, or HRQoL across all time points.

The peer mentors commented that the programme was comprehensive, equipping them with the knowledge and ability needed to mentor exercise for people with MCI. They reported that the programme was meaningful, enabling them to contribute to society while benefitting themselves by maintaining physically and cognitively active. They perceived the training programme as highly practical with the use of simple exercise equipment. Some peer mentors considered the pre-exercise educational module crucial because they did not have prior experience dealing with individuals with MCI. They highlighted the practical tips regarding motivating older adults and the role-play sessions for practising appropriate communication with and responses to people with MCI. They commented that the BRAVE app was a helpful resource for obtaining necessary information about MCI and exercise. They provided positive feedback about the exercise videos, which were helpful for their own practice and for motivating people with MCI. Some peer mentors suggested arranging group exercises according to participants' abilities such that those with similar abilities would be scheduled in the same session. Additionally, peer mentors preferred greater autonomy in leading the exercise sessions.

People with MCI were highly satisfied with the programme, with a mean satisfaction score of 46.16 out of 50. The item with the highest satisfaction was related to the overall programme design, whereas the item with the lowest satisfaction was the programme length (Table). They commented that the programme was comprehensive and resourceful, thereby raising their awareness of MCI and dementia and strategies for maintaining cognitive function. They described the exercise protocol as highly feasible and enjoyable. They valued the in-person and group format of the exercise sessions, which allowed interactions between other groupmates, peer mentors, and the coach. The BRAVE programme enabled social connections in the community, thereby motivating engagement in long-term exercise habits. Participants can practise the exercises at home, particularly during the COVID-19 pandemic. Some participants perceived the exercises as challenging and difficult to memorise and follow certain movements.

Discussion

The BRAVE programme effectively improved working memory, processing speed, and executive function in people with MCI. However, there were no significant improvements in global cognition, short-term memory, or HRQoL.

The most promising cognitive benefit of the BRAVE programme was improvement in executive function. Impairment in executive function is a strong predictor of progression from MCI to dementia. Executive function encompasses inhibition, working memory, and mental flexibility, which are essential higher-order neurocognitive skills to maintain independence in daily living. Meta-analyses found that exercise interventions have significant but small effect size in improving executive function among people with MCI.[1,2] The effect was superior in our study, because our programme included well-trained peer mentors to support its delivery. Peer-assisted or peer-led exercise interventions are effective in enhancing physical activity adherence among healthy older adults.[3] Two pilot studies examining peer-assisted exercise interventions among individuals with subjective memory complaints[4] and/or MCI[5] reported significantly greater therapeutic effects on executive function, memory and attention,[4] and physical activity levels in exercise groups compared with health education groups.[5] The involvement of peer mentors increased the levels of interactive communication and social interaction, thereby providing social connections and engagement for participants. This may have led to enhanced motivation and larger, more sustainable effects on cognition. The exercise protocol comprised mainly aerobic and resistance training with increasing intensity, as recommended by international guidelines for cognitive improvement in older adults. The exercises were designed to facilitate self-practice without requiring special exercise equipment. This enabled participants to continue exercising after the training period.

We did not detect significant between-group differences in global cognition and short-term memory. These findings are inconsistent with those of other exercise intervention studies. The discrepancy may be related to the use of different tools for global cognition measurement. The

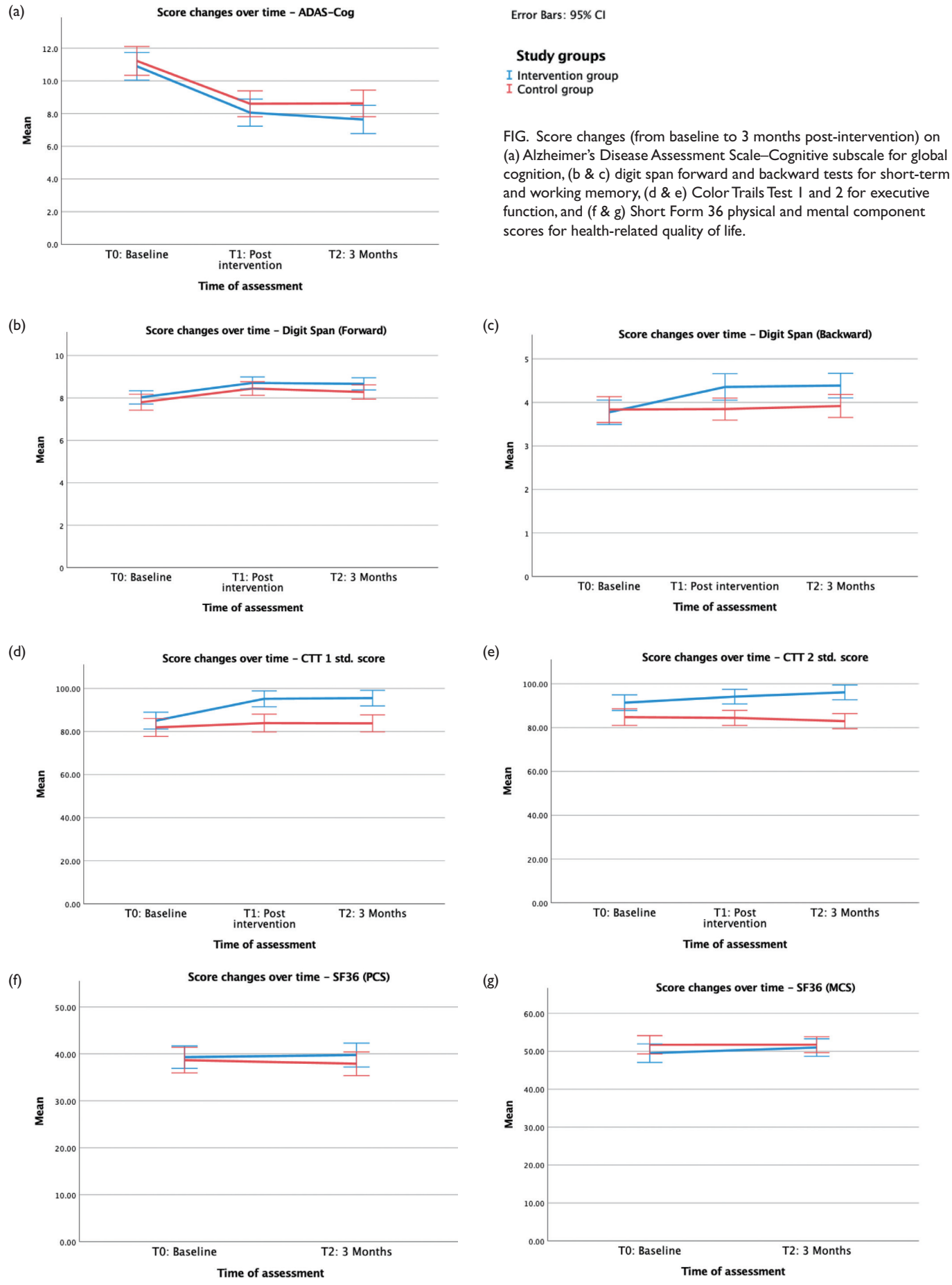

FIG. Score changes (from baseline to 3 months post-intervention) on (a) Alzheimer's Disease Assessment Scale–Cognitive subscale for global cognition, (b & c) digit span forward and backward tests for short-term and working memory, (d & e) Color Trails Test 1 and 2 for executive function, and (f & g) Short Form 36 physical and mental component scores for health-related quality of life.

TABLE. Participant satisfaction with the Brain Vitality Enhancement programme

Item	Score*
1. I understand the purpose of this programme.	4.55±0.60
2. I understand the content of this programme.	4.57±0.58
3. After completion of this programme, I can better understand how this topic relates to me.	4.59±0.57
4. The content in the programme provides me with tangible information which can be integrated into my daily life.	4.60±0.56
5. After completion of this programme, I will implement the suggestions and incorporate them into my daily life.	4.54±0.73
6. The interactive methods in this programme encouraged my participation.	4.66±0.56
7. Instructors/speakers are happy to answer my queries.	4.72±0.53
8. The programme length is commensurate with the content.	4.46±0.63
9. Overall, I am very satisfied with the programme.	4.77±0.54
10. I am willing to recommend this programme to my friends.	4.66±0.56
Overall	46.16±4.49

* Data are presented as mean±standard deviation

Alzheimer's Disease Assessment Scale–Cognitive subscale was developed to assess drug treatment efficacy in people with Alzheimer's disease; its application in the non-dementia population may be affected by its suboptimal sensitivity.

We successfully trained cognitively normal adults to support the delivery of the BRAVE programme. The peer mentors were fully equipped with the knowledge and skills needed to mentor exercise sessions for people with MCI. They can be further trained to promote active ageing. The peer mentors were of similar age to the people with MCI; this facilitated social connections and acceptance between them. Additionally, the use of scenario-based and role-playing teaching techniques enabled the peer mentors to actively acquire mentoring and communication skills.

Considering the high numbers of app downloads and content views, the BRAVE app may serve as a standalone scalable intervention for promoting brain health among older adults, with the support of family members and trained peer mentors. This is particularly relevant in the post-COVID-19 era, in which there is increasing acceptance of communication technology to provide health information and interventions.

The BRAVE programme is highly feasible and acceptable for people with MCI. Although an active lifestyle has beneficial effects on brain health promotion, the existing health and social care system lacks a structured and comprehensive method for empowering people with MCI to integrate an active lifestyle into their daily routines for long-term benefits. Peer mentors are social capital. The BRAVE programme is an effective social care service that supports self-fulfilling experience and promotes active ageing in Hong Kong.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#01170728). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

Disclosure

The results of this research have been previously published in:

1. Li PWC, Yu DSF, Siu PM, Wong SCK, Chan BS. Peer-supported exercise intervention for persons with mild cognitive impairment: a waitlist randomised controlled trial (the BRAin Vitality Enhancement trial). Age Ageing 2022;51:afac213.
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Home care programme for post-discharge older adults: abridged secondary publication

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KEY MESSAGES

1. A home care programme was established to enhance self-care continuity, chronic disease management, emotional well-being, and quality of life for post-discharge older adults in Hong Kong.
2. The WINTER Health Ambassador Toolkit were developed by health, social, and academic experts. Training workshops were provided to volunteers.
3. Both health ambassadors and care recipients gained a better understanding of healthy lifestyles, especially during cold seasons.
4. The programme has potential for reducing the numbers of emergency room visits and hospitalised days of care recipients.

Hong Kong Med J 2024;30(Suppl 5):S30-2
HMRF project number: 01170948

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Introduction

We developed the WINTER Health Ambassador Toolkit care and recruited volunteers to attend structured training workshops. The volunteers delivered healthcare intervention that empowers care recipients to promote their health and quality of life. The applicability and effectiveness of the home care model was evaluated.

Methods

The WINTER Health Ambassador Toolkit was developed by health, social, and academic experts. Volunteers aged ≥18 years were recruited in collaboration with health resource centres. Potential volunteers were interviewed to assess their motivation, relationship-building skills, and communication skills. Eligible volunteers were required to attend a training workshop and register in the Hospital Authority before implementation of the home care service.

Training workshop materials were developed with reference to existing volunteer home visit programmes. The workshop aimed to empower health ambassadors to become competent in (1) delivering home care assessment and educational services, (2) facilitating access to community resources, and (3) connecting older adults (in person and through information sharing) to community nurse services and/or social care. Ongoing support was provided to the health ambassadors.

The WINTER health home visit programme comprised four monthly visits (December 2018 to March 2019); it was expanded to six monthly visits (November 2019 to April 2020). Home care service recipients were older adults aged ≥65 years who had been discharged from hospital and required community nursing support. The first home visit mainly focused on greeting and relationship building. Care recipients were assessed to determine functional and risk profiles. In subsequent visits, educational materials and advice for self-care management in cold weather were provided. Health ambassadors contacted the care recipients by telephone approximately 2 weeks after each visit to follow up. After each visit, the health status of care recipients was reviewed and feedback from the health ambassadors was collected.

The competence (knowledge, attitude, and confidence) of health ambassadors in providing home care services was assessed before and after the training workshop using self-administered questionnaires, as were their experiences, satisfaction, and feedback. The effects of the home visit programme on care recipients' health status, health-related quality of life, and self-management skills were also evaluated. Health ambassadors assessed the care recipients' self-reported health outcomes, functional and risk profiles, and self-care behaviours.

Care recipients were compared with non–care recipients (data extracted from inpatient records)

in terms of healthcare utilisation outcomes (ie, the numbers of emergency room visits and hospitalised days within the follow-up period). Associations between home care visits and healthcare utilisation outcomes were determined using Poisson regression analysis.

Results

The WINTER Health Ambassador Toolkit comprised (1) home visit workflow, (2) health screening instruments, and (3) educational materials and advice for older adults (Table 1).

Of the 317 health ambassadors enrolled and trained, 34.4% were from the existing hospital volunteer team, including retired nurses and hospital staff; 22.7% were members of the Hong Kong Jockey Club Volunteer Team; and the remaining were from educational institutes. Eventually, 261 (82.3%) health ambassadors provided home care services.

In total, 278 older adults received 752 home visits and 1668 phone calls. Of 147 home visits that revealed either clinical or social problems, 73 showed inadequate treatment compliance and resulted in health education and reinforcement of treatment compliance from health ambassadors; 29 showed symptom exacerbation and resulted in referrals to community nurses for timely management; and 45 required financial aid or self-care supports and resulted in referrals to medical social workers at health resource centres.

Among the health ambassadors before and after the training workshop, the mean overall knowledge score improved from 7.6±0.8 to 7.7±0.8 ($P<0.05$), whereas the mean confidence scores were similar (82.3±12.7 vs 82.4±12.5). Over 90% of health

TABLE 1. Key components of the WINTER Health Assessment Toolkit

Key components
Home visit workflow
Monthly home visits and phone follow-ups over 4 months (round 1) and 6 months (round 2)
Health screening instruments
Past medical history
Physical well-being in terms of vision (Amsler grid), hearing, ambulation, frailty scale, and fall history
Emotional health measured by the 4-item Geriatric Depression Scale
Functional status measured by the Barthel Index for activities of daily living and the Lawton Instrumental Activities of Daily Living Scale
Self-perceived health status and health-related quality of life measured by the EQ-5D-5L Hong Kong version
Lifestyle behaviour in terms of smoking habits, drinking habits, home safety alarm usage, vaccination record (seasonal influenza and pneumococcal vaccines), exercise habits, eating habits, social life
Vital signs in terms of body temperature, blood pressure, pulse, respiratory rate, body weight, self-monitored blood sugar level (if applicable), pain score (if applicable), oxygen saturation level (if applicable), and risk of recurrent congestive heart failure/chronic obstructive pulmonary disease (if applicable)
Educational materials and advice for older adults
Volunteer guidelines (roles and responsibilities of volunteers, rules and regulations for home visits, communication skills tips, contingency plans)
Precautions for cold weather: warm (keep warm), immunisation (influenza vaccination), nutrition (balanced diet), tender (emotional support), exercise (regular exercise and fall prevention), and reducing risk of admission (chronic disease management)
Overview of common chronic illnesses (causes, common symptoms, assessment, advice for patients): chronic obstructive pulmonary disease, congestive heart failure, hypertension, diabetes mellitus, and chronic pain

TABLE 2. Healthcare utilisation among home care recipients and non–home care recipients

Healthcare utilisation	Non–home care recipients (n=620)	Home care recipients (n=155)	Relative risk (95% confidence interval)	P value
No. of emergency room visits	0.94±1.52	0.74±1.43	0.79 (0.65-0.97)	<0.05
Resulting in hospitalisation	0.65±1.10	0.51±1.15	0.78 (0.61-0.99)	<0.05
Not resulting in hospitalisation	0.28±0.77	0.23±0.69	0.82 (0.57-1.18)	>0.05
No. of hospitalised days during the 4 months	5.8±12.4	4.5±10.4	0.78 (0.72-0.84)	<0.001
Admission through emergency room	3.6±8.4	4.0±10.2	1.10 (1.00-1.20)	<0.05

ambassadors were satisfied with training workshop experiences and provided positive feedback in terms of their knowledge and confidence. Moreover, 94% of health ambassadors indicated that they would join similar home care services in the future. Regarding personal growth, the level of subjective social status did not improve significantly (5.7±1.7 vs 5.9±1.7). However, the improvement was greater among those involved in the first round of the programme (5.4±1.8 vs 5.8±1.8, P<0.05) and among male volunteers (5.2±1.6 vs 5.7±1.9, P<0.05).

Among the care recipients, 84% were more aware of their health and 80% felt more capable of self-care management; 99% would receive home care services in the future. Regarding health status before and after the home visit programme, care recipients had no significant improvement in activities of daily living (17.6±3.9 vs 17.5±4.4, P=0.946), instrumental activities of daily living (11.7±5.4 vs 12.2±5.6, P=0.089), or 4-item Geriatric Depression Scale scores (0.8±1.0 vs 0.7±1.2, P=0.530), but their health-related quality of life (measured by the EQ-5D-5L Hong Kong version) significantly improved by 0.056 (95% confidence interval [CI]=0.101-0.010).

Compared with non–care recipients, care recipients had 21% (95% CI=3%-35%) fewer overall emergency room visits, 22% (95% CI=1%-39%) fewer hospitalisations, and 22% (95% CI=16%-28%) fewer overall hospitalised days, but 10% (95% CI=0%-20%) more hospitalised days after admission through emergency rooms (Table 2). There was no significant difference in the number of emergency room visits that did not result in hospitalisation (P=0.287).

Discussion

Home care services improve the knowledge and social capital of volunteers, the health status of care recipients, and the capacity of the health system. Although care recipients' health-related quality of life significantly improved after home visits, the improvement did not constitute a minimally important difference.[1-3] This may be due to the COVID-19 pandemic; care recipients may have a more negative mental health status than expected. Regarding lifestyle behaviours, significantly more care recipients used home safety alarms, which may reduce health risks by connecting with health professionals.[4] Care recipients reported less loneliness, indicating that they benefited from the home visits and telephone contacts by volunteers, even during the pandemic.[5] Our findings suggest that home care visits can reduce emergency room visits and hospitalisations, while enabling early identification of acute problems, consistent with a study that showed that patient education could reduce emergency room use.[6] Home care service can expand the capacity of the healthcare workforce and healthcare system.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#01170948). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

Disclosure

The results of this research have been previously published in:

1. Lai FTT, Wong ELY, Tam ZPY, et al. Association of volunteer-administered home care with reduced emergency room visits and hospitalisation among older adults with chronic conditions: a propensity-score-matched cohort study. Int J Nurs Stud 2022;127:104158.

Acknowledgements

We thank the community outreach service teams of Prince of Wales Hospital, Alice Ho Miu Ling Nethersole Hospital, and North District Hospital for referring eligible older adults to our home visit programme and providing clinical support, the health resource centres of these hospitals for implementing the programme with the research team, and the older adults and volunteers for their participation.

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Financial incentives to promote preventive care: abridged secondary publication

J Lian *, MKH Yap, S McGhee, J Liang, R Sum, M Ryan, Q Liao

KEY MESSAGES

1. Vouchers are a financial incentive that reduce user fees for preventive services in the private sector. Older people preferred vouchers with attributes of flexibility, no expiry date, and a transparent list of service charges. These attributes could potentially influence the acceptance and use of the vouchers by older people who were willing to trade off some voucher's financial value for these attributes.
2. As a financial incentive for flu vaccination, a lottery draw was less preferred by older adults, compared with cash or a shopping voucher. Older adults were willing to trade off some of the reward amount in exchange for a reminder about flu vaccination.

Hong Kong Med J 2024;30(Suppl 5):S33-5
HMRF project number: 03170117

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Introduction

Hong Kong has an ageing population. To contain increases in healthcare costs and to maintain high quality of life for older persons, adoption of healthy behaviours and preventive services should be encouraged. Factors affecting health-related behaviours include monetary, temporal, and psychological costs and benefits. The 2017 Nobel Prize winner for Economics, Professor Richard Thaler, introduced the concept of 'nudging' people towards more appropriate behaviour using incentives.[1] In behavioural economics, there are financial and non-financial incentives. This study focuses on the financial incentive.

The Elderly Health Care Voucher Scheme aims to encourage older adults aged ≥65 years to access private primary care services for curative and preventive care. An interim report showed that 82.4% of older adults used the vouchers for acute curative services, whereas only 7% used the vouchers for preventive services.[2] Financial incentives are effective in promoting healthy behaviours, especially for one-time actions such as screening and vaccination. Financial incentives are largely affected by the characteristics of the incentive programme and the consumers.[3] Whether financial incentive works for older people and what components of financial incentive are preferred by them remain unknown.

Discrete choice experiments (DCEs) are increasingly used by health economists to explore stated preferences. DCE describes hypothetical scenarios that consist of key attributes (ie, characteristics) with varying levels for each attribute. By asking individuals to choose among scenarios that combine different levels of each attribute, the DCE elicits preferences in terms of the relative importance of each attribute. This study investigated the relative preferences of older adults regarding various attributes of financial incentives for preventive care and explored whether these preferences varied according to sociodemographic characteristics and health status.

Methods

This was a cross-sectional study using a DCE questionnaire, which was designed in three stages: identification of attributes and their levels, DCE experimental design to establish choice sets, and questionnaire development and piloting. Three preventive services were used to elicit older adults' preferences for financial incentives. Three sets of DCEs were designed to elicit older adults' preferences for (1) financial incentives in terms of a voucher for an optometric examination and general health check, and (2) a financial reward for flu vaccination. A cross-sectional study of older adults attending elderly centres across 18 districts in Hong Kong was conducted via face-to-face interviews using the DCE questionnaire.

Optometric examinations and general health checks are provided by private practitioners. Therefore, the financial incentive considered in these two scenarios constituted a new voucher to

reduce user fees for an optometric examination (or a general health check) at a private practice. This voucher involved five attributes: type (flexible for any preventive service type vs specific to one preventive service), value, expiry (with vs without expiry date), reminder about the service (reminder vs none), and list of transparent charges (charge list vs none). A forced choice method was used to present the choice set to participants without providing an opt-out option. An orthogonal design was selected for the DCE. To determine the main effect of the orthogonal design, the Hahn and Shapiro catalogue was used to reduce the full factorial design of 64 profiles to a fractional factorial design of eight profiles. Older adults were asked to consider a new voucher with different profiles (a combination of attributes with levels) that they would prefer to use for an optometric examination (or a general health check) in each choice set.

Currently, flu vaccination is provided free of charge in the public sector or with a subsidy per dose for private doctors. Therefore, the financial incentive considered was a financial reward to nudge the older adults to receive a flu vaccine. The financial reward involved three attributes: type (cash vs shopping voucher vs lottery draw), value, and reminder about flu vaccination (reminder vs none). An unforced choice method was used to present the choice set to participants (ie, choice A vs B vs neither). To determine the main effect of the orthogonal design, the Hahn and Shapiro catalogue was used to reduce the full factorial design of 24 profiles to a fractional factorial design of 16 profiles. These 16 profiles were randomly split into two blocks with eight choice sets in each block, and each participant was asked to complete only one block.

A DCE questionnaire was developed to collect information regarding previous utilisation of preventive services, the DCE choice sets for financial incentives, sociodemographic characteristics, history of chronic disease, self-perceived health, and awareness of the importance of preventive care. The questionnaire was tested for two rounds before the pilot test and for another two rounds before survey implementation.

The sample size was estimated based on Orme's rule-of-thumb. In accordance with recommended practice for conjoint analysis,[4] a minimum of 125 participants was required for two alternatives in the trade-offs, with a maximum of four levels per attribute and eight choice sets for each participant. Orme updated this theory in 2000, recommending at least 300 participants to ensure an adequate choice scenario combination.[5] We aimed to recruit at least 600 participants to enable subgroup analyses and adjustment for a possible 20% non-participation rate. Elderly centres across 18 districts in Hong Kong were randomly selected for recruitment until the target sample size for each district was reached. Individuals aged ≥65 years attending the selected elderly centres with eligibility to receive the vouchers were invited to participate. Participants were asked to complete the DCE choice sets for incentives for two out of the three preventive services, which were randomly allocated to them using block randomisation. Multinomial logit models were used to analyse the DCE data. The marginal willingness for a trade-off between the value of the voucher amount and other attributes was calculated. Subgroup analyses were conducted to explore whether preferences for attributes and their levels varied according to participant characteristics.

Results

Of 80 elderly centres approached, 20 agreed to participate and helped to recruit 770 older adults. Among these older adults, 731 confirmed participation and completed the DCE questionnaire.

All five attributes of the financial incentive of a voucher for an optometric examination were statistically significant. The positive coefficient of the value attribute indicated that respondents preferred a higher voucher value. The magnitude of the coefficient (β) showed the change in utility in moving from the reference level to the preferred level. Older adults preferred a voucher flexible for any preventive service (β=0.83), with no expiry date (β=0.53), with a transparent list of charges from the service provider (β=0.47), and with a reminder (β=0.21). They were willing to trade off HK$741 for a voucher with flexibility, HK$473 for a voucher with no expiry date, HK$420 for a voucher with a transparent list of service charges, and HK$188 for a voucher with a reminder. These preferences were consistent across subgroups for all attributes except the reminder, which was not important to the group receiving Comprehensive Social Security Allowance (CSSA) and the group with no chronic disease.

All five attributes of the financial incentive of a voucher for a general health check were statistically significant. Older adults were willing to trade off HK$587 for a voucher with a flexibility, HK$516 for a voucher with no expiry date, HK$405 for a voucher with a transparent list of service charges, and HK$167 for a voucher with a reminder. These preferences were consistent across subgroups for all attributes except the reminder, which was not important to men and the group with no chronic disease.

All three attributes of the financial reward for flu vaccination were statistically significant. Older adults preferred a higher value of reward (β=0.00755). Using cash as the reference, older adults preferred a shopping voucher as the reward type (β=0.14, P=0.048) and showed less preference towards a lottery draw (β= –0.65, P<0.001). Older adults preferred to have a reminder about the

service (β=0.77, P<0.001); they were willing to trade off HK$102 for the reminder. In subgroup analyses, these preferences were consistent for all attributes, except that the group without CSSA preferred the shopping voucher (β=0.18, P<0.05) rather than cash.

Discussion

Generally, older adults preferred a voucher for optometric examination or general health check flexible for any preventive service, with no expiry date, with a reminder, with a transparent list of charges from the service provider, and with a higher monetary value. They were willing to trade off HK$167 to 741 of the voucher amount for these attributes.

Regarding the financial reward, older adults showed less preference towards a lottery draw as the reward type. They preferred a higher reward amount and were willing to trade off HK$102 for a reminder for vaccination.

Conclusion

Vouchers for preventive services that have a flexible type, no expiry date, and a transparent list of service charges were preferred by older adults; they were willing to trade off some of the financial value to obtain these attributes. Older adults were less keen on a lottery draw as an incentive for a flu vaccination; they were willing to trade off some of the reward amount for a reminder to get flu vaccination.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#03170117). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

Disclosure

The results of this research have been previously published in:

1. Liao Q, Lau W, McGhee S, et al. Barriers to preventive care utilization among Hong Kong community-dwelling older people and their views on using financial incentives to improve preventive care utilization. Health Expect 2021;24:1242-53.

Acknowledgements

We thank the staff of 20 participating elderly centres for assistance with recruitment and logistical arrangements. We also thank Prof Mandy Ryan and her team members from the Health Economics Research Unit, The University of Aberdeen, United Kingdom for providing training and guidance for DCEs.

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Incidence and mortality of sepsis in Hong Kong between 2009 and 2018 based on electronic health records: abridged secondary publication

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KEY MESSAGES

1. Sepsis causes one in four deaths among adults in Hong Kong and affects eight in 1000 adults annually.
2. The incidence and mortality rate of sepsis in Hong Kong increased from 2009 to 2018. The mortality rate reached 47% among patients with sepsis complicated by multiorgan failure.
3. Objective clinical data from electronic health records provide more accurate sepsis surveillance compared with administrative coding.

Hong Kong Med J 2024;30(Suppl 5):S36-9
HMRF project number: 18190381

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Introduction

In Hong Kong, septicaemia is among the top 10 causes of death, with an estimated annual incidence of 296.1 per 100 000.[1] Administrative codes from hospital discharge databases or death certificates are commonly used to estimate the sepsis burden. However, these methods lack sensitivity and have low specificity.[2] A more accurate and objective approach involves analysing electronic health records (EHRs) for clinical markers of infection and concurrent organ dysfunction. We used our previously validated EHR-based surveillance to determine age- and sex-adjusted standardised estimates of sepsis incidence and mortality among adults in Hong Kong between 2009 and 2018; we also compared the performance of this method with that of administrative methods.[3]

Methods

Using the Clinical Data Analysis and Reporting System, we applied our sepsis definition to all adults (age ≥18 years) admitted to the 41 public hospitals in Hong Kong between 1 April 2009 and 31 March 2019. Adult sepsis events were defined using the estimated Sequential Organ Failure Assessment (SOFA) score.[3,4] Sepsis was defined as clinical evidence of (1) presumed infection: any microbiological culture and antibiotic treatment within ±2 calendar days of the index culture date continued for at least 4 days (unless death or hospital discharge occurred before the fourth day); and (2) concurrent acute organ dysfunction: an increase of ≥2 points in SOFA score within ±2 calendar days of the index culture date, with the prehospital SOFA score as baseline. SOFA

scores were calculated based on prehospital and hospital laboratory data, vasopressor drug records, and (rarely) diagnostic/procedural codes. Hospital episodes involving presumed infection but an increase of <2 points in SOFA score were classified as 'uncomplicated infection'. The 'all infection' group included all 'uncomplicated infection' cases and all 'sepsis' cases. Microbiological samples collected for infection control purposes were not used to determine infection status.

To compare differences in estimated sepsis burden, we applied four additional administrative methods (implicit, explicit, Martin, and local sepsis codes) and two variations of the EHR-based definition to the same dataset. The two variations of the EHR-based definition included 'no prehospital SOFA score' (only using an in-hospital SOFA score of ≥2 to identify sepsis) and 'only objective data' (using clinical data [eg, bilirubin level, platelet count, creatinine level, Glasgow Coma Scale score, the ratio of partial pressure of oxygen in arterial blood to the fraction of inspiratory oxygen concentration, and vasopressor drug records] but not diagnostic/procedural codes to calculate SOFA scores).

Two physicians, both blinded to the EHR method, independently reviewed medical records for 500 hospital episodes to determine presence of sepsis. The performances of the different surveillance methods were assessed in terms of sensitivity, specificity, positive and negative predictive values, and area under the curve (AUC); physician consensus served as the gold standard.

Mortality was defined as all-cause mortality at hospital discharge. Standardised estimates of sepsis incidence and mortality were adjusted for age and sex, with the 2008 population structure as reference. Relative annual changes in estimated incidence and mortality were modelled by exponential regression. Case fatality risk (CFR) was calculated by dividing the number of all-cause deaths at hospital discharge by the total number of cases. The proportions of sepsis-related deaths were calculated by dividing the numbers of all-cause sepsis-related deaths by all deaths among Hong Kong population, all hospital episodes, and all infections. Differences in AUCs were assessed using the DeLong test. A P value of <0.05 was considered statistically significant.

Results

We analysed 13 540 945 adult hospital episodes involving 2 928 757 patients to identify sepsis cases during the study period. Among these episodes, there were 2 373 393 (17.5%) all infection cases, including 1 888 852 (14.0%) uncomplicated infection cases and 484 541 (3.6%) sepsis cases. Overall, 54.9% of sepsis cases requiring either mechanical ventilation or vasopressors were managed in general wards, rather than in intensive care units (ICUs). Among the sepsis cases, those managed in general wards had a higher mortality rate, compared with those admitted to ICUs (54.3% vs 30.0%, P<0.001). Sepsis cases with ≥4 organ dysfunctions (8.9%) had the highest CFR (47.3%); 43.2% of sepsis cases had two organ dysfunctions and a CFR of 18.4%.

Our EHR-based sepsis surveillance method showed that sepsis incidence from 2009 to 2018 increased from 623 to 756 per 100 000 (relative increase of 2.8%/year, P<0.001), whereas sepsis mortality increased from 142 to 156 per 100 000 (relative increase of 1.9%/year, P=0.002) [Fig 1]. The implicit method (relative decrease of 2.9%/year, P<0.001) and the explicit method (relative decrease of 4.0%/year, P=0.001) indicated decreases in sepsis incidence, as did sepsis mortality when the implicit method (relative decrease of 2.8%/year, P=0.001) and the explicit method (relative decrease of 4.8%/year, P<0.001) were used. Between 2009 and 2018, sepsis CFR slightly declined from 23.0% to 21.6% (relative decrease of 0.5%/year, P=0.03) [Fig 2]. A greater reduction in CFR from 3.0% to 2.4% (relative decrease of 2.2%/year, P<0.001) was observed among all hospital episodes. The proportion of sepsis-related deaths increased among all deaths (relative increase of 3.9%/year, P<0.001) [Fig 2].

The sensitivities of administrative methods ranged from 5% to 15%, compared with 84% for the EHR-based definition. In contrast, the specificities of the EHR-based and administrative methods were consistently ≥96%. The EHR method had the highest AUC (0.91) for distinguishing sepsis among all infection cases, compared with other methods (P<0.001). The implicit and explicit methods had AUCs of 0.55 and 0.52, respectively.

Discussion

In 2018, the standardised sepsis incidence in Hong Kong was 756 per 100 000, which is similar to rates in Sweden (780) and Taiwan (772); higher than rates in France (403), China (422), Spain (445), England (102), New Zealand (107), Norway (140), Brazil (290), and South Korea (453); and much lower than rates in Australia (1163) and Malawi (1772). Administrative methods demonstrated low sensitivity (15%) and thus greatly underestimated sepsis incidence in Hong Kong. In contrast, the EHR method displayed 84% sensitivity and 99% specificity. Our EHR-based estimates of sepsis incidence were generally higher than those reported in studies that used administrative methods alone such as studies from France, Spain, South Korea, Brazil, Norway, and New Zealand. In contrast, our estimates of sepsis incidence were similar to those reported in studies from Sweden and Beijing, which used objective clinical data.

The low sensitivity of administrative methods may be attributable to Hong Kong–specific factors

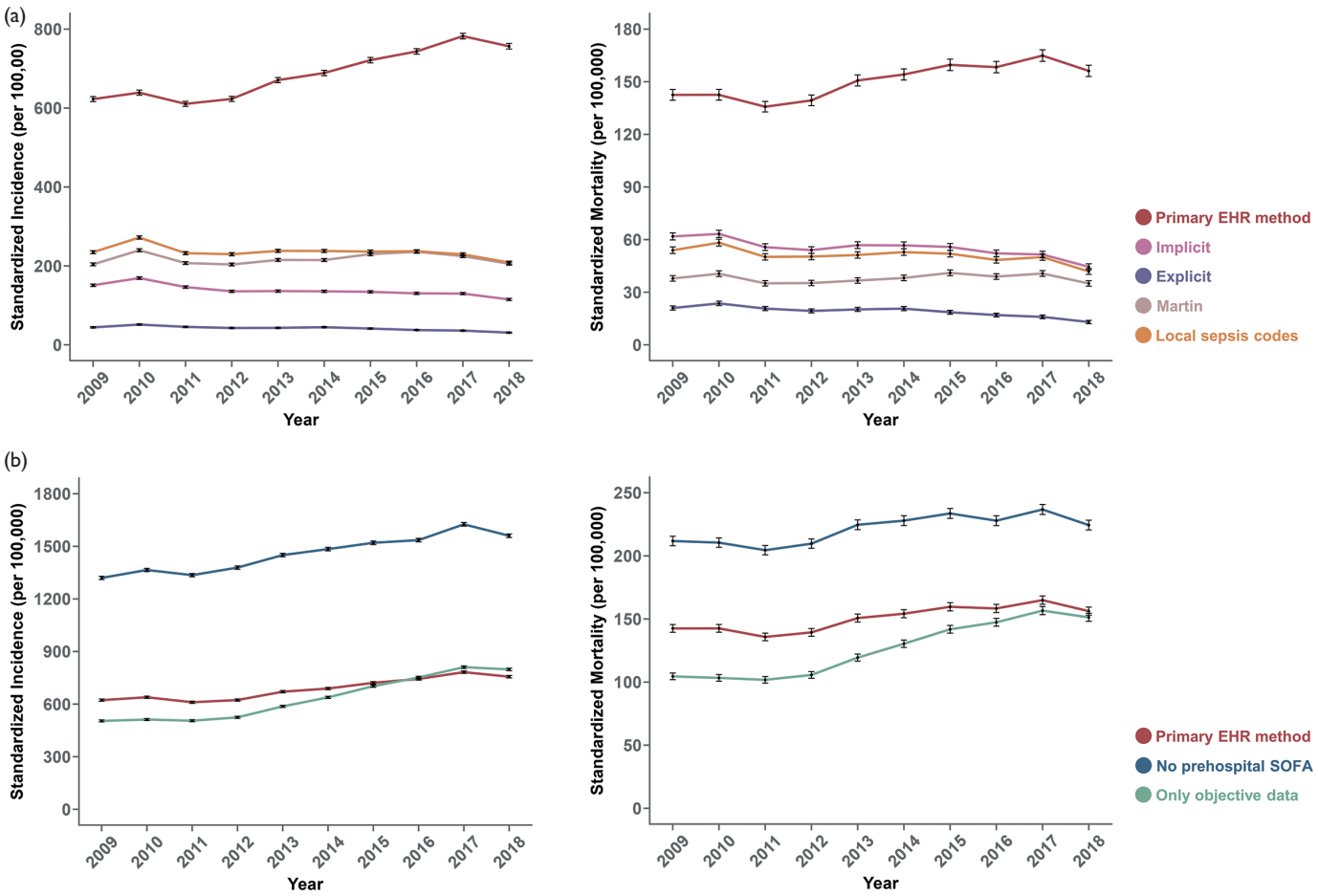

FIG 1. Age- and sex-adjusted standardised estimates of sepsis incidence and mortality in Hong Kong from 2009 to 2018, based on our electronic health record (EHR) method, compared with (a) four other administrative methods (implicit, explicit, Martin, and local sepsis codes) and (b) two variations of our EHR method ('no prehospital Sequential Organ Failure Assessment [SOFA] score' and 'only objective data').

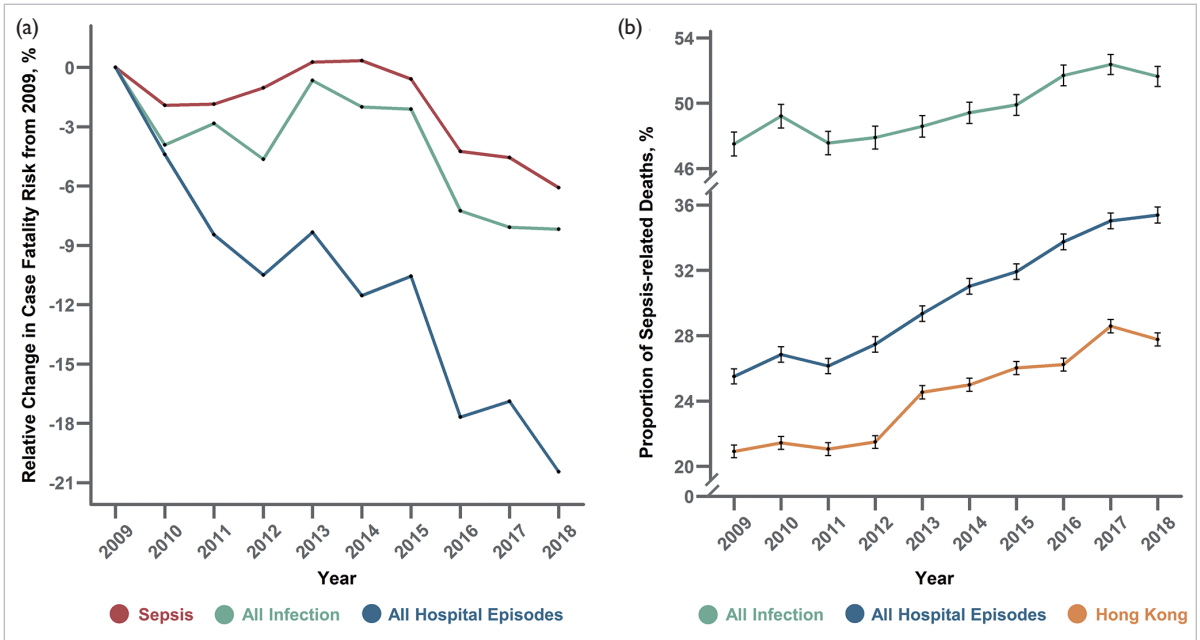

FIG 2. (a) Relative changes in case fatality risk for sepsis, all infections, and all hospital episodes at discharge from 2009 to 2018. (b) Annual proportions of sepsis-related deaths among all infection deaths, all hospital episode deaths, and all Hong Kong deaths.

such as the lack of dedicated coding teams, inadequate training in diagnostic coding, and independence from public healthcare funding. Notably, objective data regarding prescriptions for antihypertensive drugs and diagnostic codes for hypertension exhibited discrepancies in Hong Kong's population health database. In the United States, changes in coding practices and sepsis awareness over time have contributed to increases in reported sepsis incidence and declines in CFR estimated by administrative methods, compared with estimated by objective clinical data.[5] Our results highlight the potential for confounding when different sepsis surveillance methods are used without robust validation.

In 2018, 27.8% of all deaths in Hong Kong were at least partly attributable to sepsis. This percentage is at least 20% higher than official statistics based on death certificates, which combine pneumonia and septicaemia. Sepsis is increasingly becoming the primary cause of death because the slight improvement in sepsis CFR (relative decrease of 0.5%/year) has lagged behind the pace of overall improvement in survival from other diseases.

Hong Kong faces a substantial healthcare resource deficit in treating sepsis, considering that 54.9% of sepsis cases requiring vasopressors or mechanical ventilation were managed in general wards, rather than in ICUs. Only 12.9% of sepsis cases were managed in ICUs, likely because few ICU beds were available; this rate is much lower than the 54.7% reported in the United States but similar to the 17.1% reported in Japan and 13.8% reported in Beijing. Our results highlight the need to increase critical care provision in Hong Kong to match the sepsis burden, as timely ICU admission may improve sepsis survival rates.

Conclusions

Sepsis constitutes a major health challenge in Hong Kong, with one in four deaths attributable to sepsis. An expansion of critical care services is necessary to address the rising incidence and mortality rates of sepsis. Our findings demonstrate the feasibility and advantages of an EHR-based approach for sepsis surveillance.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#18190381). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

Disclosure

The results of this research have been previously published in:

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Data driven identification and classification of Chinese medicine syndrome types among functional dyspepsia patients: latent tree analysis (abridged secondary publication)

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KEY MESSAGES

1. Eight pattern differentiation rules for functional dyspepsia were derived by latent tree analysis using data from 250 and 150 patients in Hong Kong and Hunan, respectively.
2. At least one traditional Chinese medicine diagnostic pattern was identified in 70.7%, 73.6%, and 64.0% of the participants in the overall (n=400), Hong Kong (n=250), and Hunan (n=150) samples, respectively.
3. Cold-heat complex (59.8%) and liver qi invading the stomach (77.1%) were the most prevalent diagnostic patterns in Hong Kong and Hunan samples, respectively.
4. Spleen-stomach deficiency cold was highly likely to co-exist with spleen-stomach qi deficiency.
5. Participants with severe anxiety tended to exhibit liver qi invading the stomach.

Hong Kong Med J 2024;30(Suppl 5):S40-6
HMRF project number: 03170027

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Introduction

Functional dyspepsia (FD) is a disorder of gut-brain interaction characterised by postprandial fullness, early satiety, epigastric burning, and/or epigastric pain. These symptoms are unexplainable by routine gastrointestinal examinations such as oesophagogastroduodenoscopy and *Helicobacter pylori* testing. Predominant postprandial fullness and early satiety are classified as postprandial distress syndrome (PDS), a subtype of FD, whereas predominant epigastric burning and epigastric pain are classified as epigastric pain syndrome (EPS), another subtype of FD. Patients with FD may also exhibit an overlapping PDS and EPS subtypes.

The symptoms of FD resemble those of stomach pain and stomach stuffiness and fullness, observed in traditional Chinese medicine (TCM). Herbal medicine is recommended, and its effectiveness has been supported by network meta-analyses.[1,2] A key difference between TCM and conventional medicine is that treatment strategies in TCM are guided by pattern differentiation, which involves comprehensive analysis of a patient's clinical features to determine the location, cause, and nature of disease. Nonetheless, standardised rules for pattern differentiation have not been established for any medical conditions. Thus, the TCM diagnostic process is likely to have low inter-rater agreement, leading to substantial variations in diagnostic-to-treatment decisions and quality of care. The incorporation of pattern differentiation into TCM clinical research is also hindered by the lack of standardised TCM diagnostic instruments. Variations in TCM diagnostic patterns across

different clinical and geographical characteristics suggest that the use of a single standardised diagnostic instrument is not always appropriate.

In this diagnostic cross-sectional study of FD patients, we aimed to (1) establish score-based differentiation rules using latent tree analysis, (2) identify co-existing TCM diagnostic patterns and their distributions, (3) assess associations between TCM diagnostic patterns for FD and common comorbidities, and (4) compare the prevalences of individual TCM diagnostic patterns in Hong Kong and Hunan, as well as geographical variations in clinical features constituting the same patterns.

Methods

We recruited consecutive patients with FD who presented to the gastrointestinal outpatient departments of Prince of Wales Hospital in Hong Kong (n=250) or Xiangya Hospital in Hunan (n=150) between December 2020 and May 2021. Patients were screened for eligibility by trained TCM practitioners; medical records were then reviewed to confirm eligibility. Inclusion criteria were (1) completion of oesophagogastroduodenoscopy within 10 years with *H pylori*–negative results, or a history of *H pylori* positivity with completed eradication therapy; (2) presence of symptoms that met the reference standard for FD without subtype restrictions (ie, PDS, EPS, or overlapping); (3) age ≥18 years; and (4) provision of written informed consent. Exclusion criteria were (1) a diagnosis of organic oesophageal or gastric disease within the preceding month (including oesophagitis, gastro-oesophageal reflux disease, peptic ulcer, and predominant heartburn or acid regurgitation); (2) presence of unremoved stomach polyps; (3) a history of major abdominal surgery (ie, appendectomy, gastrectomy, gastric lymph node removal, cholecystectomy, or abdominal cancer removal); (4) pregnancy at the time of enrolment; (5) presence of major physical illness (ie, malignancy or serious infection); or (6) refusal to provide written informed consent.

Participants were asked to complete an online questionnaire consisting of four sections. The first section collected data regarding basic demographic and clinical characteristics. The second section evaluated FD subtype (using the Ford et al reference standard for FD) and irritable bowel syndrome status (using the Rome IV Diagnostic Questionnaire for Adult Functional Gastrointestinal Disorders). The third section contained a 55-item Traditional Chinese Medicine Clinical Feature Questionnaire for Functional Dyspepsia (TCMQ-FD), which was designed to collect self-reported clinical feature data. Participants were asked to rate the severity of each clinical feature on a five-point Likert scale; a higher numerical rating indicated greater severity. To facilitate identification of TCM diagnostic patterns, the questionnaire items were developed using two sources: (1) a systematic review of TCM diagnostic instruments for FD[3] and (2) the 2017 Chinese Medicine Expert Consensus on Functional Dyspepsia Diagnosis in China. The fourth section assessed psychiatric comorbidities and disease-specific quality of life. Depression and anxiety symptoms were measured by validated Chinese versions of the Patient Health Questionnaire-9 and General Anxiety Disorder-7, respectively. Disease-specific quality of life was evaluated using the validated Chinese version of the Nepean Dyspepsia Index (NDI).

Data of TCMQ-FD from the overall (n=400), Hong Kong (n=250), and Hunan (n=150) samples were used to derive score-based pattern differentiation rules for TCM diagnostic patterns for FD. Latent tree analysis,[4] a quantitative approach consisting of five steps (Table 1), was conducted only for the overall sample. Pattern differentiation rules were derived for all three samples using soft labels.[5] Multivariate regression analyses were performed to assess correlations between individual TCM diagnostic patterns and between TCM diagnostic patterns and clinical and geographical variables.

Results

The basic characteristics of participants are presented in Table 2. Eight TCM pattern differentiation rules for FD were derived (Table 3): (1) spleen deficiency and qi stagnation, (2) cold-heat complex, (3) stomach heat, (4) liver qi invading the stomach, (5) spleen-stomach dampness-heat, (6) spleen-stomach qi deficiency, (7) spleen-stomach deficiency cold, and (8) spleen deficiency with dampness encumbrance. Using the derived pattern differentiation rules, at least one TCM diagnostic pattern was identified in 70.7%, 73.6%, and 64.0% of participants in the overall (n=400), Hong Kong (n=250), and Hunan (n=150) samples, respectively. Two or more diagnostic patterns were identified in 59.6% and 52.7% of participants in the Hong Kong and Hunan samples, respectively.

Spleen deficiency with dampness encumbrance was the most common TCM diagnostic pattern; its prevalence was 56.2%. Cold-heat complex and liver qi invading the stomach were the most common TCM diagnostic patterns in the Hong Kong (59.8%) and Hunan (77.1%) samples, respectively. Spleen-stomach dampness-heat was the least prevalent diagnostic pattern.

Of 14 pairs of TCM diagnostic patterns with positive association, three demonstrated exceptionally high adjusted odds ratios (AORs) [>5.00]: spleen-stomach deficiency cold plus spleen-stomach qi deficiency (AOR=53.23, 95% confidence interval [CI]=21.77-130.16) and their reverse pairing (AOR=49.61, 95% CI=20.96-117.44), spleen

TABLE 1. Latent tree analysis for traditional Chinese medicine (TCM) diagnostic patterns

Step	Procedure
Statistical pattern discovery	Build three independent global latent tree models in the Lantern software, choose the model with the best Bayesian information criterion score for subsequent steps, and obtain probabilistic co-occurring clinical features from each latent variable
Statistical pattern interpretation	Examine quantitative relationships between latent variables and clinical features constituting potential patterns by checking relevant probability distributions in the Lantern software, determine the TCM diagnostic pattern connotations for latent variables from a clinical perspective based on TCM expertise, and generate a list of potential TCM diagnostic patterns
Traditional Chinese Medicine diagnostic pattern identification	Based on TCM expertise, select only potential TCM diagnostic patterns that contain all essential clinical features for subsequent steps; discard patterns that do not contain all essential clinical features
Traditional Chinese Medicine diagnostic pattern quantification	Construct a latent tree model for each selected TCM diagnostic pattern in the Lantern software
Traditional Chinese Medicine pattern differentiation rule derivation	Use latent tree models to classify participants, assign a soft label to each participant based on the probability of exhibiting each TCM diagnostic pattern, and derive score-based differentiation rules according to a Naïve Bayes approach

TABLE 2. Baseline characteristics of participants

Baseline characteristic	Hong Kong sample (n=250)	Hunan sample (n=150)
Age, y	51.4±13.0	45.2±13.7
No. (%) of women	199 (79.6)	101 (67.3)
Body mass index, kg/m^2	20.8±7.7	22.1±4.6
Duration of symptoms, y	3.6±5.3	2.3±3.4
Functional dyspepsia symptom subtype		
Postprandial distress syndrome only	70 (28.0)	28 (18.7)
Epigastric pain syndrome only	18 (7.2)	28 (18.7)
Overlapping	162 (64.8)	94 (62.6)
Self-reported duration of symptoms, y		
≥5	57 (22.8)	18 (12.0)
<5	193 (77.2)	132 (88.0)
Patient Health Questionnaire score	7.0±4.9	7.1±6.4
Depression (cut-off=10)	67 (26.8)	51 (34.0)
Generalised Anxiety Disorder score¶	5.8±5.3	6.6±5.7
Anxiety (cut-off=10)	47 (18.8)	41 (27.3)
Nepean Dyspepsia Index		
Symptom severity	44.8±27.7	53.6±32.6
Eating/drinking	64.0±23.2	68.9±24.4
Sleep	62.9±29.6	67.8±30.0
Knowledge/control	70.2±21.0	67.7±24.7
Interference	69.3±20.0	70.2±21.7
Total quality of life score	66.6±20.0	68.6±21.6
Concomitant irritable bowel syndrome	45 (18.0)	26 (17.3)

deficiency and qi stagnation plus spleen-stomach deficiency cold (AOR=8.73, 95% CI=3.52-21.68) and their reverse pairing (AOR=8.66, 95% CI=3.52-21.30), and spleen deficiency and qi stagnation plus cold-heat complex (AOR=6.07, 95% CI=2.86-12.90) and their reverse pairing (AOR=6.03, 95% CI=2.84-12.80).

Compared with Hunan sample, Hong Kong sample was more likely to experience spleen deficiency and qi stagnation (AOR=2.59, 95% CI=1.05-6.40), spleen deficiency with dampness encumbrance (AOR=2.34, 95% CI=1.15-4.74), and cold-heat complex (AOR=2.23, 95% CI=1.18-4.21). Compared with participants with the overlapping subtype, those with the PDS subtype were more likely to have spleen-stomach qi deficiency (AOR=3.20, 95% CI=1.07-9.59). Participants with liver qi invading the stomach were likely to have a higher burden of anxiety symptoms (AOR=1.20, 95% CI=1.08-1.33). Regarding disease-specific quality of life, participants with spleen deficiency and qi stagnation (AOR=1.03, 95% CI=1.01-1.05) and stomach heat (AOR=1.02, 95% CI=1.01-1.03) were more likely to have higher NDI symptom severity. Participants with spleen-stomach deficiency cold (AOR=1.04, 95% CI=1.01-1.07) and spleen-stomach dampness-heat (AOR=1.03, 95% CI=1.01-1.05) were more likely to have a higher quality of life in terms of eating and drinking. Participants with spleen deficiency with dampness encumbrance (AOR=1.04, 95% CI=1.01-1.06) were likely to have better knowledge and control over dyspeptic symptoms.

Discussion

At least one of the eight TCM pattern differentiation rules for FD was identified in 70.7% of the overall sample. However, the clinical appropriateness of this diagnostic approach should be validated in consultations, during which diagnostic decisions can be confirmed, adjusted, or rejected based on

TABLE 3. Score-based differentiation rules of traditional Chinese medicine diagnostic patterns for functional dyspepsia in the three samples

Overall sample (n=400)		Hong Kong sample (n=250)		Hunan sample (n=150)	
Clinical feature	**Score**	**Clinical feature**	**Score**	**Clinical feature**	**Score**
Spleen deficiency and qi stagnation					
Distension and fullness in the stomach	5.5	Distension and fullness in the stomach	7.6	Distension and fullness in the stomach	3.5
Oppression in the chest	4.2	Oppression in the chest	5.3	Lack of strength	2.9
Lack of strength	3.6	Lack of strength	4.1	Reluctance to speak	2.8
Reluctance to speak	3.6	Reluctance to speak	3.9	Oppression in the chest	2.6
Torpid intake	2.2	Torpid intake	1.8	Torpid intake	2.6
Lassitude of spirit	1.9	Belching	1.5	Lassitude of spirit	2.5
Belching	1.5	Lassitude of spirit	1.4	Belching	1.4
Unformed stools	0.9	Unformed stools	0.8	Unformed stools	0.8
Cold-heat complex					
Signs and symptoms exacerbated by pressure	6.9	Signs and symptoms exacerbated by pressure	7.6	Borborygmus	8.3
Borborygmus	6.5	Borborygmus	6.0	Signs and symptoms exacerbated by pressure	6.0
Bitter taste in the mouth	4.7	Bitter taste in the mouth	5.5	Vomiting and nausea	4.0
Signs and symptoms exacerbated by ingestion	4.3	Signs and symptoms exacerbated by ingestion	5.5	Bitter taste in the mouth	4.0
Gastric upset	4.0	Gastric upset	4.4	Unformed stools	3.2
Vomiting and nausea	3.5	Vomiting and nausea	3.1	Signs and symptoms exacerbated by ingestion	3.1
Unformed stools	3.0	Unformed stools	2.9	Gastric upset	2.5
Signs and symptoms exacerbated by cold	2.5	Signs and symptoms exacerbated by cold	2.7	Dry mouth	2.4
Dry mouth	2.2	Dry mouth	1.9	Signs and symptoms exacerbated by cold	2.2
Stomach heat					
Burning sensation in the stomach	9.6	Bitter taste in the mouth	8.5	Burning sensation in the stomach	7.7
Acid vomiting	8.5	Burning sensation in the stomach	7.7	Acid vomiting	6.9
Bitter taste in the mouth	7.7	Acid vomiting	6.2	Bitter taste in the mouth	6.6
Gastric upset	4.1	Fetid mouth odour	4.9	Gastric upset	5.6
Dry mouth	3.8	Gastric upset	3.7	Dry mouth	4.2
Fetid mouth odour	3.4	Dry mouth	3.6	Swift digestion with rapid hungering	2.7
Swift digestion with rapid hungering	3.2	Swift digestion with rapid hungering	3.6	Constipation	2.6
Yellowish urine	2.6	Yellowish urine	3.0	Fetid mouth odour	2.0
Constipation	2.4	Constipation	2.2	Poor sleep quality	2.0
Poor sleep quality	1.8	Poor sleep quality	1.7	Yellowish urine	1.8
Liver qi invading the stomach					
Depressed mood	10.7	Depressed mood	11.9	Depressed mood	7.0
Oppression in the chest	7.6	Oppression in the chest	8.3	Oppression in the chest	5.7
Acid vomiting	5.8	Acid vomiting	7.8	Acid vomiting	4.3
Irritability	4.7	Irritability	4.9	Irritability	4.2
Vomiting and nausea	3.5	Distension and fullness in the hypochondrium	3.3	Vomiting and nausea	4.0
Distension and fullness in the hypochondrium	3.4	Vomiting and nausea	2.9	Signs and symptoms exacerbated by mood	3.6
Signs and symptoms exacerbated by mood	2.9	Signs and symptoms exacerbated by mood	2.7	Distension and fullness in the hypochondrium	3.0
Hiccup	2.1	Distension and fullness in the stomach	0.7	Belching	2.5
Distension and fullness in the stomach	1.1	Hiccup	0.6	Hiccup	2.2
Belching	0.5	Belching	-0.3	Distension and fullness in the stomach	1.7

TABLE 3. (cont'd)

Overall sample (n=400)		Hong Kong sample (n=250)		Hunan sample (n=150)	
Clinical feature	**Score**	**Clinical feature**	**Score**	**Clinical feature**	**Score**
Spleen-stomach dampness-heat					
Tenesmus	7.6	Tenesmus	8.1	Tenesmus	6.9
Passing stools with difficulty	5.0	Passing stools with difficulty	6.1	Unformed stools	4.0
Unformed stools	4.8	Unformed stools	5.3	Diarrhoea	3.8
Foul-smelling stools	3.9	Foul-smelling stools	4.4	Passing stools with difficulty	3.4
Diarrhoea	3.4	Diarrhoea	3.3	Foul-smelling stools	3.1
Yellowish urine	2.0	Borborygmus	2.2	Yellowish urine	1.8
Borborygmus	1.9	Yellowish urine	2.1	Vomiting and nausea	1.4
Vomiting and nausea	1.4	Thirst without desire to drink	1.6	Borborygmus	1.1
Thirst without desire to drink	1.0	Vomiting and nausea	1.4	Torpid intake	-0.4
Torpid intake	-0.1	Torpid intake	0.0	Thirst without desire to drink	0.0
Spleen-stomach qi deficiency					
Reluctance to speak	8.6	Lack of strength	9.9	Lack of strength	6.2
Lack of strength	8.1	Reluctance to speak	8.8	Reluctance to speak	5.5
Stomach heaviness	5.5	Sallow complexion	6.5	Stomach heaviness	4.6
Sallow complexion	5.4	Stomach heaviness	5.4	Sallow complexion	4.1
Undigested food in stools	3.8	Undigested food in stools	4.6	Lassitude of spirit	4.0
Hard stools followed by soft stools	3.8	Hard stools followed by soft stools	4.5	Weight loss	3.1
Weight loss	3.0	Foul-smelling stools	2.7	Hard stools followed by soft stools	2.9
Lassitude of spirit	2.9	Lassitude of spirit	2.6	Undigested food in stools	2.8
Foul-smelling stools	2.3	Weight loss	2.3	Torpid intake	2.6
Unformed stools	1.6	Signs and symptoms relieved by pressure	1.9	Foul-smelling stools	1.8
Signs and symptoms relieved by pressure	1.6	Unformed stools	1.8	Unformed stools	1.4
Torpid intake	1.3	Torpid intake	0.4	Signs and symptoms relieved by pressure	1.2
Spleen-stomach deficiency cold					
Reluctance to speak	8.1	Lack of strength	8.0	Reluctance to speak	5.3
Lack of strength	6.5	Reluctance to speak	7.3	Lack of strength	5.0
Sallow complexion	3.9	Sallow complexion	4.6	Body heaviness	3.5
Body heaviness	3.4	Bland taste in the mouth	3.6	Lassitude of spirit	3.4
Bland taste in the mouth	2.9	Body heaviness	3.3	Sallow complexion	3.1
Lassitude of spirit	2.7	Lassitude of spirit	2.4	Torpid intake	2.5
Dull pain in the stomach	2.1	Cold hands and feet	2.2	Bland taste in the mouth	2.2
Aversion to cold	2.1	Dull pain in the stomach	2.1	Aversion to cold	2.1
Cold hands and feet	1.8	Aversion to cold	2.1	Dull pain in the stomach	1.9
Signs and symptoms exacerbated by cold	1.7	Signs and symptoms exacerbated by cold	2.0	Signs and symptoms exacerbated by cold	1.5
Signs and symptoms relieved by pressure	1.5	Signs and symptoms relieved by pressure	1.8	Cold hands and feet	1.4
Torpid intake	1.2	Unformed stools	0.7	Signs and symptoms relieved by pressure	1.2
Unformed stools	0.8	Torpid intake	0.5	Unformed stools	0.9
Spleen deficiency with dampness encumbrance					
Unformed stools	5.2	Unformed stools	5.4	Tenesmus	4.7
Tenesmus	4.8	Bland taste in the mouth	5.4	Unformed stools	4.6
Bland taste in the mouth	4.4	Tenesmus	4.9	Bland taste in the mouth	3.5
Excessive phlegm or salivation	4.4	Excessive phlegm or salivation	4.8	Foul-smelling stools	3.5
Foul-smelling stools	3.8	Passing stools with difficulty	4.3	Excessive phlegm or salivation	3.5
Vomiting and nausea	3.7	Foul-smelling stools	3.9	Vomiting and nausea	3.3
Passing stools with difficulty	3.6	Vomiting and nausea	3.8	Diarrhoea	3.0
Heavy-headedness	3.2	Heavy-headedness	3.4	Heavy-headedness	2.7
Dizziness	2.7	Dizziness	3.4	Passing stools with difficulty	2.5
Diarrhoea	2.7	Foreign body sensation in the throat	2.6	Borborygmus	2.3
Borborygmus	2.5	Borborygmus	2.5	Foreign body sensation in the throat	2.2
Foreign body sensation in the throat	2.5	Body heaviness	2.5	Body heaviness	2.2
Body heaviness	2.4	Diarrhoea	2.4	Dizziness	2.0
Thirst without desire to drink	1.6	Thirst without desire to drink	1.5	Thirst without desire to drink	1.6
Torpid intake	0.8	Torpid intake	0.5	Torpid intake	1.2

additional information from physical examinations, as well as pulse and tongue assessments. TCM diagnostic patterns for FD could be incorporated into computer-aided TCM diagnostic systems. This could streamline clinical decision-making by generating patient-specific recommendations based on clinical information and comorbidities, improve quality of care through accurate diagnoses and treatments, and update TCM practitioners about new evidence on diagnostic methods and treatment strategies. Nevertheless, implementation assessments are necessary to evaluate the capacity and preparedness of TCM practitioners and healthcare organisations in adopting these digital health applications.

There are limitations to this study. First, the TCMQ-FD only considers clinical features from the preceding 2 weeks; it may not capture the dynamic nature of TCM diagnostic patterns. Therefore, patients should complete the questionnaire immediately before follow-up consultations to facilitate accurate diagnoses. Second, although pulse and tongue features are essential for TCM diagnosis, these were not included in the latent tree analysis because of the lack of automated diagnostic apparatuses to objectively acquire such data. Third, the pattern differentiation rules derived from Hong Kong and Hunan samples may not be generalisable populations outside of these two regions. Fourth, climate may influence the distribution of TCM diagnostic patterns in a geographical region; the results might have differed if this study were conducted in summer when dampness is the dominant qi of the season.

To address these limitations, future research should focus on developing instruments that can reliably quantify tongue and pulse diagnostic features. Next, multicentre diagnostic cross-sectional studies should be conducted to collect TCMQ-FD data along with instrument-measured pulse and tongue data for assessment of geographic variation in TCM diagnostic patterns. Sampling and data collection during different seasons would help to quantify possible variability in diagnostic patterns attributable to climate factors. Incorporation of validated TCM diagnostic instruments into artificial intelligence–powered electronic health records could facilitate continuous monitoring of intra-patient diagnostic changes and support the development of prognostic models to inform treatment decisions.

Although the latent tree analysis demonstrated good performance in this study, its applicability among more complex patients with higher co-morbidity burdens is unclear. For example, in patients with dual complaints of FD and anxiety disorder, it is unclear whether the use of TCMQ-FD alone is sufficient, or whether an additional anxiety disorder–specific TCM diagnostic instrument is needed. According to classical TCM theory, both FD and anxiety disorder may share a common pathogenesis of liver qi stagnation, suggesting that TCMQ-FD may be sufficient to guide treatment. However, when a patient presents with two distinct complaints (eg, FD and knee osteoarthritis), a separate TCM diagnostic tool is probably necessary. From a practical perspective, TCM practitioners need to prioritise which condition to address, considering the patient's preferences and values. Therefore, clinician experience and judgement remain essential for TCM diagnosis.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#03170027). The full report is available from the Health and Medical Research Fund website (https://rfs2.healthbureau.gov.hk).

Disclosure

The results of this research have been previously published in:

1. Ho L, Xu Y, Zhang NL, et al. Quantification of prevalence, clinical characteristics, co-existence, and geographic variations of traditional Chinese medicine diagnostic patterns via latent tree analysis-based differentiation rules among functional dyspepsia patients. Chin Med 2022;17:101.
2. Ho L, Zhang NL, Xu Y, et al. Latent tree analysis for the identification and differentiation of evidence-based traditional Chinese medicine diagnostic patterns: a primer for clinicians. Phytomedicine 2022;106:154392.
3. Ho L, Chung VC, Wong CH, et al. Evaluating traditional Chinese medicine diagnostic instruments for functional dyspepsia: systematic review on measurement properties. Integr Med Res 2021;10:100713.

Acknowledgements

We thank the Department of Gastroenterology, Xiangya Hospital of Central South University, and the Medical Specialist Outpatient Clinic, Prince of Wales Hospital for arranging patient recruitment in Hunan and Hong Kong, respectively. We also thank the Henan University of Chinese Medicine and the Department of Computer Science and Engineering, The Hong Kong University of Science and Technology, for providing expertise in latent tree analysis.

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