

# Secondary prevention of fragility fractures: instrumental role of a fracture liaison service to tackle the risk of imminent fracture

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## ABSTRACT

The occurrence of fragility fractures is strongly associated with significant morbidity and mortality. Effective recommendations should be set to treat these patients punctually for secondary prevention of fractures and ultimately decrease healthcare costs. The key pitfalls in the current management for patients with fragility fractures are the lack of fracture liaison services, low prescription rates for osteoporosis, inadequate referral for rehabilitation, and low follow-up attendance leading to poor compliance with treatment. Most imminent fractures occur within the first 2 years, and it is therefore important to raise the awareness of fracture risk and provide fracture liaison services to improve management. Fracture liaison services are coordinated and have been shown to be cost-effective. These services allow prompt identification of patients with fragility fractures. This leads to appropriate investigations of their bone health and fall risk. Information about and interventions for

each patient are provided for secondary prevention of fractures. Implementation of the fracture liaison services model would play a major role in improving patient outcomes in our community.

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## Introduction

Osteoporosis is a socio-economic threat, and with the ageing population, the disease has grown into a global epidemic. The lifetime fracture risk in patients with osteoporosis can reach 40%, and the most common fracture regions are the hip, distal radius, and spine.<sup>1</sup> In Hong Kong, the number of fragility fractures is on the rise, and hospital budgets are increasing. Currently, around 6000 hip fractures occur annually in Hong Kong, and these numbers are projected to double by 2050.<sup>2</sup> A recent study showed that the number of hip fractures in Asia will increase from 1 124 060 in 2018 to 2 563 488 in 2050, a 2.28-fold increase.<sup>3</sup> It is also expected that 50% of hip fractures will occur in Asia, with the majority in China.<sup>4</sup>

According to the Osteoporosis Society of Hong Kong, 95% of direct costs of osteoporosis are incurred for acute management and rehabilitation of the fracture.<sup>5</sup> Annual hospital expenditures for hip fractures in Hong Kong amount to approximately US\$52 million and rising.<sup>6</sup>

The occurrence of fragility fractures is strongly associated with significant morbidity and mortality. Mortality after a hip fracture is around 5% to 10% after

1 month, and one-third of patients die by 1 year.<sup>7</sup> At least 10% of patients have care issues, and most have residual disability and pain. Many studies have also shown that mortality after vertebral compression fractures is almost as high as that after hip fractures.<sup>8</sup> More importantly, after the occurrence of the first fracture, prompt measures and initiatives should be taken for secondary prevention to decrease healthcare costs.

The single most predictive factor of a fragility fracture is the presence of a previous fracture. The relative risk is approximately 2-fold higher to sustain a hip or vertebral fracture after a prior fragility fracture. The risk of vertebral fracture is 4-fold higher for patients with prior vertebral fractures than for those without.<sup>9</sup> The increased relative risk is not constant with time or age, as imminent fractures occur shortly after the initial one.<sup>10</sup> A previous large-scale prospective cohort study in Australia showed that absolute repeat fracture risk persists up to 10 years and that 40% to 60% of surviving patients experience a subsequent fracture. However, 41% of refractures in women and 52% of refractures in men occur within the first 2 years.<sup>11</sup> Effective recommendations should be made to treat

## 脆性骨折的二次預防：骨折聯絡服務降低二次骨折風險的作用

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脆性骨折有極高的發病率和死亡率。對於這類患者應給予及時有效的二次骨折預防的相關指導，從而最終減輕醫療負擔。目前關於脆性骨折患者管理最主要的問題在於缺乏骨折聯絡服務、骨質疏鬆處方率低、康復轉介缺乏，以及低隨訪率導致的依從性不高等。大部份的二次骨折發生在首次骨折後兩年內，因此提高患者的骨折預防意識並提供有效骨折聯絡服務對這類患者的管理很重要。骨折聯絡服務是一項多部門相互協調且能實現最大效益的措施。這些服務首先可以及時識別脆性骨折患者，繼而能夠對他們的骨骼健康和跌倒風險進行有效評估。因此通過整合患者資料並採取相應干預措施可有效預防二次骨折。骨折聯絡服務對改善本地骨折患者的治療成效非常重要。

these patients punctually for secondary prevention of fractures and ultimately decrease healthcare costs in Hong Kong.

This guideline serves to provide recommendations about identifying patients with risk of imminent fracture. Prompt management with the incorporation of fracture liaison services (FLS) based on a review of the current literature is provided.

### Pitfalls in Hong Kong's current fragility fracture management

The PubMed database (date last accessed: 28 October 2018) was searched. The keywords used for the search criteria were “fragility fracture” and “Hong Kong” and “manage\*”. Seven studies were retrieved in the initial search. From these results, four studies related to the management of fragility fractures in Hong Kong were included.<sup>12-15</sup> The remaining studies were unrelated and excluded. The key pitfalls in the current management of patients with fragility fractures in Hong Kong are the lack of FLS (10%-25% in public hospitals), low prescription rates for osteoporosis on discharge (23% of hip fracture cases), inadequate referral rates for rehabilitation (22% of hip fracture cases), and low follow-up attendance (35.1% of hip fracture cases at 1 year). It is therefore important to raise awareness about imminent fractures and FLS to further improve the current management situation.

Currently, there is a large treatment gap between osteoporotic fractures and secondary prevention. According to the International Osteoporosis Foundation (IOF), only 10% to 25% of public hospitals in Hong Kong have FLS.<sup>6</sup> Furthermore, a study of six hospitals in Hong Kong located in different clusters showed that only 23% of patients were prescribed anti-osteoporotic medications

postoperatively for hip fractures.<sup>15</sup> Another study showed that 33% of anti-osteoporotic medications that were prescribed were given 6 months after discharge.<sup>14</sup> Routine preoperative orthogeriatric co-management for hip fractures was given in only 3.5% of cases.<sup>15</sup> A previous study had already established certain outcomes, showing a shorter length of stay, shorter time to surgery, lower in-hospital mortality, and lower hospital cost of US\$170 224 annually with implementation of an orthogeriatric intervention for hip fracture patients in Hong Kong.<sup>16</sup> Currently, there is poor coordination among different subspecialties in delivery of post-fragility fracture care. There is also low follow-up attendance after discharge: 74.8% at 3 months and 35.1% at 1 year.<sup>15</sup> Internal surveys showed only 22% of patients are referred for rehabilitation, with inadequate fall prevention programmes provided.

As the number of patients with osteoporosis continues to grow, regular follow-up is crucial, as long-term monitoring for chronic disease is required. Currently, fewer than five public hospitals have dedicated osteoporosis clinics for care of these patients. More importantly, many patients are seen at various subspecialty clinics, including general medicine, orthopaedics, endocrinology, and geriatrics, causing the standard of care to be suboptimal.

There are currently seven dual-energy X-ray absorptiometry (DXA) scanning facilities in the public setting in Hong Kong. The average waiting time for a DXA scan is 1 to 6 years, depending on location. The long waiting time places the patient at high risk of imminent fractures occurring within 2 years of the initial fracture.

According to the Asian Federation of Osteoporosis Societies Call-To-Action Committee, osteoporosis should be made a national health priority.<sup>17</sup> It is also important to raise public awareness, have educational programmes for health professionals, and ultimately prevent secondary fractures. The current evidence suggests that a structured service delivery model (ie, an FLS) is therefore essential to improve the care of our patients. There is certainly a pressing need for further resource allocation to the prevention of secondary fractures to decrease healthcare costs, patient morbidity, and mortality.

### Preventing imminent fractures

Imminent fractures, or fractures occurring within 2 years of the initial fracture, should be identified promptly to receive anti-osteoporotic treatment and fall prevention programmes.<sup>10,18</sup> Prompt multidisciplinary assessment should be employed, and patients should undergo thorough evaluation to prevent imminent fractures. It is well documented that the cause of imminent fractures may be the

increase of frailty during hospital admission.<sup>18</sup> Immobility due to pain and disability causes an increased loss of cortical and trabecular bone.

The Reykjavik Study fracture registrar from Iceland showed that the risk of a major osteoporotic fracture after a previous one was 2.7-fold higher compared with the general population risk at 1 year, and this risk elevation decreases to 1.4-fold at 10 years.<sup>10</sup> The risk of a second major osteoporotic fracture also increases by 4% for each year of age. As the absolute risk is 6.1% for subsequent fractures at 1 year, the implementation of global fracture prevention strategies to prevent imminent fractures is crucial.<sup>10</sup> The concept of a recent fracture as a more predictive risk factor than fracture history is important for future health policies.<sup>10,19</sup> Therefore, the window of opportunity to treat imminent fractures is best taken advantage of by FLS, as it provides a holistic approach and treats osteoporosis from a public health perspective.<sup>20</sup>

### **Importance and cost-effectiveness of fracture liaison services for patients with fragility fractures**

Fracture liaison services are coordinated services that identify patients with fragility fractures, assess and treat their bone health, make referrals for rehabilitation, and aim to prevent secondary fractures.<sup>21</sup>

Most patients do not receive appropriate bone health assessment and treatment. In fact, only 9% to 50% of patients in the US, the UK, and Canada proceed with these assessments after a fragility fracture.<sup>21</sup> International FLS guidelines in the US including initiatives by specialty groups, such as the American Orthopedics Association “Own the Bone” campaign, have been established to target these patients during the imminent fracture time interval.<sup>22</sup> In a US nationwide study of 273 330 patients with index fractures, imminent fractures were common in the 1 year following hip, shoulder or wrist fractures. Therefore, national strategies to minimise further impairment have been urged, as subsequent fractures cause significant morbidity and loss of quality of life. However, many hospitals worldwide still lack this model of care.<sup>23,24</sup>

A recent meta-analysis of 74 controlled studies showed that FLS programmes improved outcomes, with significant increases in bone mineral density assessment (48.0% vs 23.5%), treatment initiation (38.0% vs 17.2%) and adherence (57.0% vs 34.1%), and reductions in re-fracture incidence (6.4% vs 13.4%) and mortality (10.4% vs 15.8%).<sup>25</sup> In Taiwan, 22 FLS programmes have already been established, of which 11 are accredited by the IOF.<sup>26</sup> Taiwan has some of the best FLS coverage in the Asia-Pacific region. Randomised controlled trials are being conducted

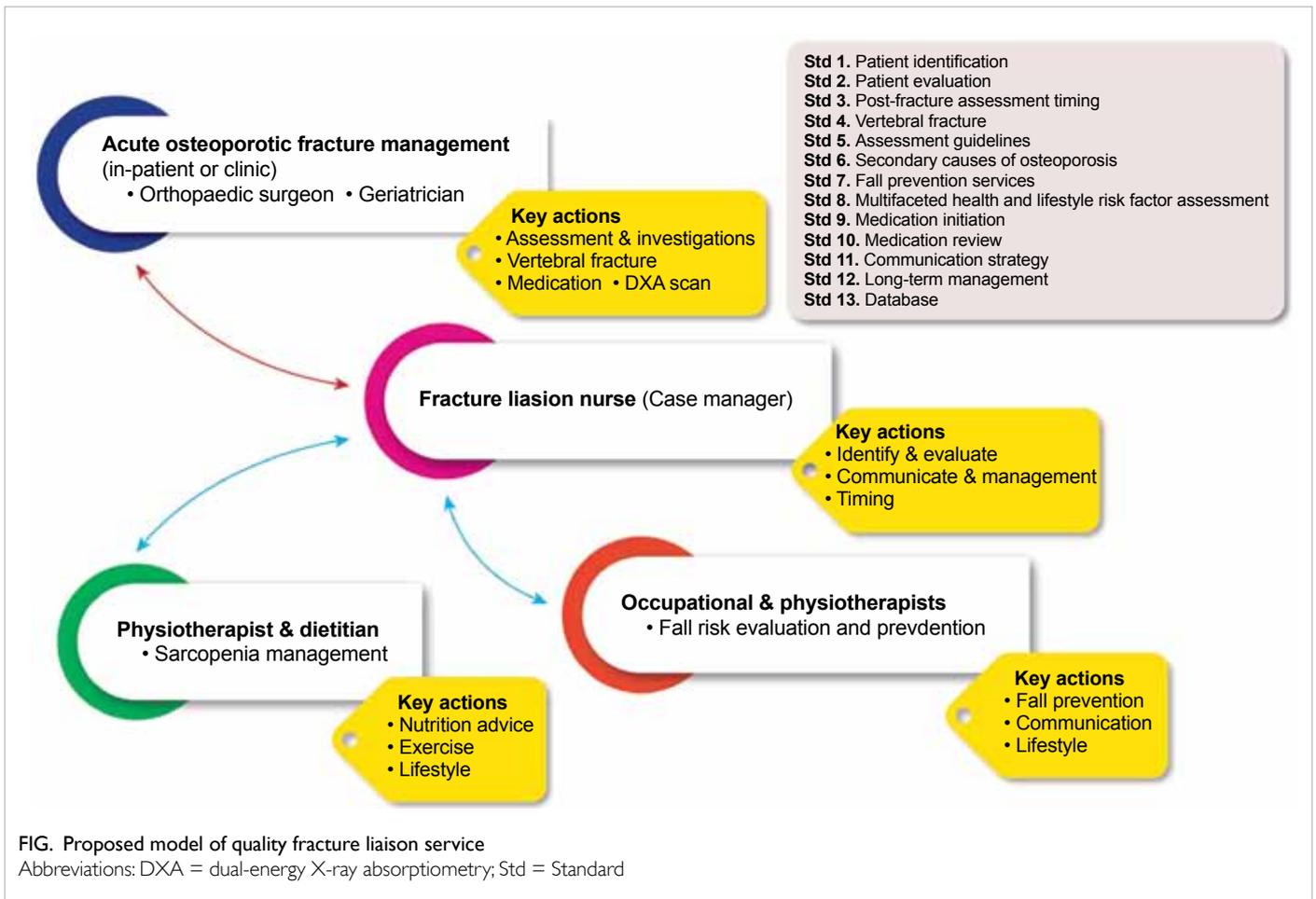
to assess outcomes in Taiwan.<sup>26</sup> Other countries that have adopted FLS programmes include Japan, where it has been proven to be cost-effective. A recent study in Japan showed an additional lifetime cost of US\$3396 per person for an additional 0.118 quality-adjusted life year (QALY), resulting in an incremental cost-effectiveness ratio of US\$28 880 per QALY gained.<sup>27</sup> Furthermore, a systematic review has also shown that FLS per the IOF Best Practice Standards conducted in Canada, Australia, the US, the UK, Japan, and Sweden were all found to be cost-effective in comparison with usual or no treatment, regardless of programme intensity or country.<sup>24</sup> The costs per QALY ranged from US\$3023 to US\$28 800 in Japan and from US\$14 513 to US\$112 877 in the US. Several studies have also shown that FLS was cost-saving, which further reinforces that these services should be widely adopted and introduced.<sup>24</sup> Fracture liaison services could effectively bridge the gap between the patient and prevention of imminent fractures.

### **Creating a model for fracture liaison services in Hong Kong**

There are several published models to create an effective model of FLS care. Many hospitals have adopted the recommendations of the IOF Capture the Fracture Campaign, which consist of 13 Best Practice Standards.<sup>28</sup> The recent FLS consensus meeting in the Asia-Pacific Region endorsed by the IOF, the Asian Federation of Osteoporosis Societies, and the Asia Pacific Osteoporosis Foundation reinforced that there is still a wide gap in terms of fragility fractures and secondary prevention.<sup>12</sup>

Therefore, it is essential to establish FLS in Hong Kong (Fig). One essential element is a dedicated coordinator, often a nurse,<sup>29</sup> who provides proactive recruitment of patients aged  $\geq 50$  years with new fragility fractures or vertebral fractures. All patients should be evaluated for future fracture risk within 3 months. In addition to DXA scanning, the cause of osteoporosis should also be recognised, and blood tests including serum calcium, phosphate, creatinine, and 25-hydroxyvitamin D should be performed to look for secondary osteoporosis. All patients with osteoporosis should be treated promptly with anti-osteoporotic medications and reviewed regularly during follow-up. Fall risk and health and lifestyle risk factors should be evaluated accordingly. A dedicated database with long-term management should be established for these patients.

The implementation of an FLS model would play a major role in improving patient outcomes to prevent imminent fractures. It is important to have policymaker and stakeholder engagement to achieve successful and widespread uptake of FLS in our community.



### Anti-osteoporotic drug use and challenges in decreasing imminent fractures

In Hong Kong, only 23% of hip patients discharged are prescribed with anti-osteoporotic medications, excluding calcium and vitamin D supplements.<sup>15</sup> An FLS model would be important to coordinate and improve on osteoporosis medication initiation and adherence and improve follow-up.<sup>30</sup> Bisphosphonates are most commonly prescribed and are currently considered first-line drugs for treatment of osteoporosis.<sup>5</sup> The Agency for Healthcare Research and Quality published a systematic review showing alendronate, risedronate, zoledronic acid, denosumab and teriparatide to be effective at reducing fractures.<sup>31</sup> This further shows the importance of early treatment to prevent imminent fractures. A meta-analysis of 10 studies of five anti-osteoporotic agents (risedronate, alendronate, strontium ranelate, zoledronic acid, and denosumab) also showed an 11% reduction in mortality with treatment for established fragility fractures. Mortality reduction was highest in patients

who were frail and older.<sup>32</sup> The Table summarises a selection of anti-osteoporotic drugs.

Currently, the prescription of combination treatment has a low quality of evidence, except for the addition of teriparatide to on-going denosumab, which produces a large increase in bone mineral density compared with monotherapy.<sup>33</sup> The use of bisphosphonates following teriparatide has been shown to produce an additional bone mineral density increase in both the hip and spine.<sup>33,34</sup> Sequential anabolic drugs followed by anti-remodelling agents may therefore become the standard to treat imminent fractures in the future.<sup>35</sup>

However, poor compliance with bisphosphonates is a major issue worldwide.<sup>18</sup> Additional measures to tackle this problem are essential to ensure successful patient care during the period of imminent fractures.

### Improving compliance with bisphosphonates

A systematic review has shown that 50% of all patients prescribed oral bisphosphonates stop treatment within 1 year.<sup>18,36</sup> Although patients receiving weekly instead of daily oral bisphosphonates had higher

TABLE. Summary of anti-osteoporotic drugs

Parameters	ZOL	ALN	RIS	PTH	DMAb
Anti-fracture efficacy					
Vertebral fracture	-70%	-45%	-39%	-65%	-68%
Non-vertebral fracture	-25%	-23%	-20%	-53%	-20%
Hip fracture	-41%	-53%	-26%	ND	-40%
Survival benefit	28%	Obs	Obs	ND	ND
CV risk	±AF	±AF	±AF	Nil	Nil
Safely administered in patients with CKD (eGFR mL/min)	>35	>30	>30	ND	No contra-indication
Frequency of administration	Yearly	Weekly	Monthly/weekly	Daily	6-Monthly

Abbreviations: AF = atrial fibrillation; ALN = alendronate; CKD = chronic kidney disease; CV = cardiovascular; DMAb = denosumab; eGFR = estimated glomerular filtration rate; ND = No data; Obs = observational study; PTH = parathyroid hormone; RIS = risedronate; ZOL = zoledronate

compliance at 1 year, the overall treatment rate was still below the required standard for optimal fracture prevention.<sup>37</sup> A meta-analysis of 15 articles describing 171 063 patients revealed a 46% increase of fracture risk in non-compliant patients compared with compliant patients.<sup>38</sup> Adherence to bisphosphonates has become a major problem leading to subsequent fractures, morbidity, and mortality.

International guidelines to improve adherence have been recommended. A systematic review showed that periodic follow-up interaction between patients and health professionals improved adherence and persistence.<sup>39</sup> A review of 20 studies showed the importance of simplification of the dosing regimen.<sup>40</sup> The Denosumab Adherence Preference Satisfaction study, a 24-month randomised, crossover comparison with alendronate in postmenopausal women, showed less frequent non-adherence with denosumab, which was injected every 6 months.<sup>41</sup> Of the 250 women who enrolled, at 1 year and 2 years, 88.1% and 92.5% adhered to denosumab, whereas only 76.6% and 63.5% adhered to alendronate, respectively. Furthermore, of the 198 subjects who expressed treatment preference, 92.4% favoured injections over oral therapy.<sup>41</sup> A US study consisting of 10 863 patients with newly initiated osteoporosis treatment showed that at 12 months of treatment, persistence varied from 28.9% to 35.1% for oral bisphosphonate users, 59.1% for teriparatide, and 68.3% for denosumab.<sup>42</sup> Although there has been no comparison between denosumab and zoledronic acid, recent reviews have shown that adherence to and patient preference for zoledronic acid were greater compared with that for oral bisphosphonates.<sup>43</sup> This further reinforces that patients prefer less frequent dosing and that switching from oral to injection therapy may improve compliance.<sup>44</sup>

Prescribing anti-osteoporotic drugs that have higher compliance is an important consideration for

clinicians, especially during the first 2 years, when imminent fracture risk is high.

### Fall prevention programmes to prevent imminent fractures

Numerous studies have concluded that among elderly people, fall prevention is as important as treating osteoporosis.<sup>45</sup> It is estimated that fall prevention reduces the number of fractures by over 50%. Fracture liaison services models have recommended assessment of fall risk, which is essential to prevent imminent fractures. Early referral for physiotherapy and exercise-based intervention (including multi-component exercises with strength, endurance, and balance training) reduces the rate and risk of falling.<sup>46</sup> Balance training is also an important component of fall prevention for patients with fragility fractures during rehabilitation. Tai chi has been shown to significantly reduce fall risk and rate.<sup>47</sup>

A recent systematic review and meta-analysis showed that vibration therapy reduced fall rate and may prevent fractures by reducing falls.<sup>48</sup> Vibration therapy provides a non-invasive, cyclic mechanical stimulation that has been shown to improve quadriceps muscle strength, balancing, and movement velocity.<sup>49</sup> Incorporating the device into multidisciplinary rehabilitation programmes for elderly patients with hip fractures has also been shown to be effective.<sup>13</sup> The FLS programme is able to integrate fall risk assessments with adequate information and treatment for patients to prevent further falls and fractures, especially during the imminent fracture period.

### Increasing awareness of sarcopenia and fragility fractures

Sarcopenia is an age-related decline in muscle bulk and strength, which is strongly associated with

frailty.<sup>50</sup> According to the practical definition and consensus for age-related sarcopenia in 2010 by the European Working Group on Sarcopenia in Older People and in 2014 by the Asian Working Group for Sarcopenia, low muscle mass and low muscle function or low physical performance are the criteria for diagnosis.<sup>51,52</sup>

Sarcopenia leads to falls, disability, and increased mortality. More importantly, a recent multi-centre cross-sectional study showed that 37% of subjects with hip fractures were diagnosed with sarcopenia.<sup>53</sup> Several studies have shown that osteoporosis is closely related to sarcopenia.<sup>54</sup> A study of 2400 Japanese women also showed sarcopenia was highly associated with osteopenia (present in 16.8% of cases) and osteoporosis (in 20.4%).<sup>55</sup>

A local study showed that the prevalence of sarcopenia was 73.6% in men and 67.7% in women with geriatric hip fractures.<sup>56</sup> This prevalence is much higher than that in community-dwelling elderly people, and therefore, the health status of muscle tissue should be investigated during hospitalisation.<sup>51</sup> A global evaluation of nutritional status is required in addition to early mobilisation of patients. Resistance exercises and supplements including vitamin D should be recommended to strengthen muscle and hence reduce falls.<sup>57,58</sup> Studies have also shown that nutrition is important for sarcopenia and that protein intake of 1.0 to 1.2 g/kg per day is recommended for older adults.<sup>59</sup> Dietary protein increases insulin-like growth factor, which has anabolic effects on bone and muscle. Furthermore, calcium absorption is increased, having positive effects on bone health.<sup>59</sup> Awareness and understanding of the condition are crucial for better care and quality of life for elderly patients.

## Recommendation to establish fracture liaison services in Hong Kong

Once an official FLS programme is established in Hong Kong based on the 13 best practice standards, serial workshops should be hosted to promote FLS expansion by a panel of local experts.<sup>26</sup> Experts should be invited as clinical instructors and coordinators to share experiences. New programmes can also share challenges and interim progress for discussion. Furthermore, osteoporosis treatment promotion events can be held at each participating hospital to allow close interactions between healthcare providers and patients. After successful implementation, accreditation by the IOF can be achieved based on assessment of the practice guidelines.<sup>60</sup>

## Conclusion

Fracture liaison service models should be adopted

in hospitals for secondary prevention of fractures, particularly imminent fractures. Fracture liaison services can improve patient outcomes and decrease healthcare costs. With the current lack of resources and pitfalls in fragility fracture management in Hong Kong, major changes and engagement with stakeholders are crucial to achieve successful and widespread uptake of FLS to tackle the undertreatment of osteoporosis.

## Author contributions

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Concept and design of study: All authors.

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Drafting of the manuscript: RMY Wong, SW Law, WH Cheung.

Critical revision for important intellectual content: KB Lee, SKH Chow.

## Conflicts of interest

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