Fracture cascade and secondary fracture prevention

Thierry Thomas
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University Hospital of Saint-Etienne, France
Please make sure to type your questions into the Questions Box!
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Disclosures

- **Fees for lectures and consultancy**
  Abbvie, Amgen, BMS, Chugai, Expanscience, Gilead, HAC-Pharma, LCA, Lilly, Medac, MSD, Pfizer, Thuasne, TEVA and UCB

- **Research grants or investigator fees**
  Amgen, Bone Therapeutics, Chugai, HAC-Pharma, MSD, Novartis, Pfizer, and UCB
Risk factors in osteoporosis

- Risk factors are numerous: BMD, previous treatment with glucocorticoids, gender, shape of bone...
- Interaction between them is complex
- Risks of low BMD and risk of fragility fracture
Prevalent fracture increases the risk of incident fracture
Prevalent fracture increases the risk of incident fracture
Risk of incident vertebral fracture in women with prevalent vertebral fracture over time

Cumulative Incidence (%)

Years following a vertebral fracture

Women
Men

Fracture cascade
Risk according to prevalent vertebral fractures number

Siris E. Osteoporos Int 2007
Clinical case 1

- Mrs Smith
- 70 years – some back pain last year
- She complains of severe pain between the shoulder blades while carrying her shopping bag
- No improvement after having taken acetamiphen
- 4 weeks later, pain decreased. 2 months later, full pain recovery. She lost 3 centimeters in height.
- She received calcium and vitamin D.
- 1 year later, she complains of acute back pain of the lower thoracic spine. Clinical examination: severe pain at the T11-T12 level
- X-Rays showed 3 vertebral fractures: T6-T9 and T11
Clinical case 1
In the year following a vertebral fracture about 20% of women will have a new vertebral fracture and about 25% will have a new fracture (VF+NVF).

Fracture cascade
An imminent risk of another fracture

Lindsay et al. JAMA 2001, 285: 320-23
Lindsay et al, Osteoporosis Int 2002 13(suppl 3) :S47, P106
Fracture cascade
An imminent risk of another fracture

The risk of both vertebral and non-vertebral fracture is increased in the year following a fracture.

Figure 1  (A) Percentage of all first (grey line) and subsequent (black line) fractures. (B) Relative risk of all subsequent fractures calculated as a mean from the first fracture (grey line) and per separate year of follow-up (black line).
Fracture cascade
Multifactorial mechanisms

Vertebral fracture

Bone properties
- Bone density
- Bone quality
- Intra-vertebral distribution of bone mass
- Micro-architectural deterioration

Spine properties

Local spine properties
- Vertebral macrostructure
- Intervertebral disc integrity
- Baseline fracture characteristics

Global spine properties
- Spinal curvature
- Spine loading
- Muscle weakness

Neurophysiologic properties
- Trunk muscle control
- Balance
- Fear and pain
- Functional mobility

Fracture cascade
The role of hyperkyphosis

Hyperkyphosis of any etiology has been associated with:

- decreased thoracic extensor muscle strength,
- unstable gait,
- increased body sway,
- decreased physical and pulmonary functions,
- chronic pain,
- increased spinal loads contributing to the vertebral fracture cascade.
Clinical case 2
Non vertebral fracture increases the risk of vertebral fracture

The risk of vertebral fracture is increased after a prevalent NVF in women over 65 years

<table>
<thead>
<tr>
<th>First fracture</th>
<th>Women 65 – 74 years</th>
<th>Women 75 - 84 years</th>
<th>Women &gt; 85 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radius / Ulna</td>
<td>2.2 (1.6-3.0)</td>
<td>1.6 (1.2-2.1)</td>
<td>1.6 (1.0-2.4)</td>
</tr>
<tr>
<td>Hip</td>
<td>3.8 (2.3-5.8)</td>
<td>2.5 (1.9-3.2)</td>
<td>1.7 (1.2-2.3)</td>
</tr>
</tbody>
</table>

1Standardised incidence ratio (SIR) and 95% confidence interval in patients > 65 ans. (data from General Practice Research Database GPRD, UK).
Clinical case 3

- Mrs Monk
- 65 years – wrist fracture after a fall from her height
- Risk factors
  - Her mother had a hip fracture
  - Smoker (10 units/day from 18 years)
  - Low BMI: 18kg/m²
- 3 years later, she felt again on her buttocks with back pain at the lower part of the thoracic level
- X-rays:
Clinical case 3
Vertebral fracture assessment by X-rays or VFA
Increased risk related to a previous non-vertebral fracture

- Fall plays a major role
Hyperkyphosis and risk of non-spine fractures in older community dwelling women

Timeline study in SOF

Adjusted HRs for Non-Spine Fracture Over 5 Years in Women Stratified by Prevalent Vertebral Fracture

Kado DM, J Bone Miner Res 2014;29:2210-16
Conservative treatment allowed to control pain evolution
Patient was discharged from the hospital 1 week later
3 years later
Fall from her height induced a trauma to the greater trochanter
Hip fracture diagnosed
### Table 1. Pooled Associations of Prior and Subsequent Fractures

<table>
<thead>
<tr>
<th>Location of prior fracture</th>
<th>Population</th>
<th>Location of subsequent fractures</th>
<th>Wrist</th>
<th>Vertebral</th>
<th>All (or nonspine)</th>
<th>Hip</th>
<th>Pooled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist</td>
<td>Peri/postmenopausal</td>
<td>3.3 (2.0, 5.3)^a</td>
<td>1.7 (1.4, 2.1)^a</td>
<td>2.4 (1.7, 3.4)^a,d</td>
<td>1.9 (1.6, 2.2)</td>
<td>2.0 (1.7, 2.4)^d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>3.6 (1.9, 6.7)</td>
<td>7.2 (3.6, 14.6)</td>
<td>2.0 (1.7, 2.4)</td>
<td>1.5 (1.3, 1.7)</td>
<td>2.6 (1.9, 3.5)</td>
<td></td>
</tr>
<tr>
<td>Vertebral</td>
<td>Peri/postmenopausal</td>
<td>1.4 (1.2, 1.7)^a</td>
<td>4.4 (3.6, 5.4)^d</td>
<td>1.8 (1.7, 1.9)</td>
<td><strong>2.3 (2.0, 2.8)</strong></td>
<td>1.9 (1.7, 2.3)^b</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>1.4 (1.1, 1.9)</td>
<td>19.0 (6.5, 55.3)</td>
<td>2.7 (1.8, 3.9)</td>
<td>2.1 (1.6, 2.7)</td>
<td>2.3 (1.8, 2.9)^b</td>
<td></td>
</tr>
<tr>
<td>(all, or specific sites)</td>
<td>Peri/postmenopausal</td>
<td>1.8 (1.3, 2.4)</td>
<td>1.9 (1.3, 2.8)^d</td>
<td>1.9 (1.3, 2.7)^d</td>
<td>2.0 (1.7, 2.3)</td>
<td>1.9 (1.7, 2.2)^d</td>
<td></td>
</tr>
<tr>
<td>Hip</td>
<td>Peri/postmenopausal</td>
<td>—^c</td>
<td>—^c</td>
<td>1.4 (1.2, 1.7)</td>
<td>2.1 (1.2, 3.5)</td>
<td>1.7 (1.4, 2.2)^d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>—^c</td>
<td>—^c</td>
<td><strong>2.5 (1.8, 3.5)</strong></td>
<td>1.9 (NA)^a</td>
<td><strong>2.3 (1.5, 3.7)^a</strong></td>
<td><strong>2.4 (1.9, 3.2)</strong></td>
</tr>
<tr>
<td>Pooled</td>
<td>Peri/postmenopausal</td>
<td>1.9 (1.3, 2.8)</td>
<td>2.0 (1.6, 2.4)^b,d</td>
<td>1.9 (1.6, 2.2)^d</td>
<td>2.0 (1.9, 2.2)</td>
<td>2.0 (1.8, 2.1)^b,d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2.3 (1.7, 3.3)</td>
<td>7.2 (3.6, 14.6)^b</td>
<td>1.8 (1.6, 2.2)</td>
<td>1.8 (1.6, 2.2)</td>
<td>2.2 (1.9, 2.6)^b</td>
<td></td>
</tr>
</tbody>
</table>
Vertebral or hip fracture risk after any fracture independent of age

Table 3. Standardized incidence ratio (SIR) of subsequent fractures stratified by age in patients aged 65 years or older

<table>
<thead>
<tr>
<th>Original fracture</th>
<th>Later fracture</th>
<th>65–74 years</th>
<th></th>
<th></th>
<th></th>
<th>75–84 years</th>
<th></th>
<th></th>
<th></th>
<th>85+ years</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Men SIR</td>
<td>Women SIR</td>
<td>Men SIR</td>
<td>Women SIR</td>
<td>Men SIR</td>
<td>Women SIR</td>
<td>Men SIR</td>
<td>Women SIR</td>
<td>Men SIR</td>
<td>Women SIR</td>
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<td>(95% CI)</td>
<td>(95% CI)</td>
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<td>(95% CI)</td>
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<td>(95% CI)</td>
<td>(95% CI)</td>
<td>(95% CI)</td>
<td>(95% CI)</td>
<td></td>
</tr>
<tr>
<td>Any fracture</td>
<td>Radius/ulna</td>
<td>6.5 (5.2–8.0)</td>
<td>2.8 (2.5–3.0)</td>
<td>4.7 (3.6–6.0)</td>
<td>2.6 (2.4–2.8)</td>
<td>2.6 (1.6–4.0)</td>
<td>1.8 (1.6–2.0)</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Femur/hip</td>
<td>5.2 (4.2–6.5)</td>
<td>3.6 (3.3–4.0)</td>
<td>4.4 (3.7–5.2)</td>
<td>2.8 (2.7–1.9)</td>
<td>2.8 (2.2–3.5)</td>
<td>1.9 (1.7–2.0)</td>
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<tr>
<td></td>
<td>Vertebral</td>
<td>5.3 (3.8–7.1)</td>
<td>2.8 (2.4–3.3)</td>
<td>3.5 (2.5–4.8)</td>
<td>2.2 (1.9–2.5)</td>
<td>2.5 (1.3–4.1)</td>
<td>1.9 (1.5–2.2)</td>
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<tr>
<td>Radius/ulna</td>
<td>Any fracture</td>
<td>6.4 (5.2–7.8)</td>
<td>3.6 (3.3–3.8)</td>
<td>4.5 (3.6–5.7)</td>
<td>2.9 (2.7–3.1)</td>
<td>3.6 (2.5–5.1)</td>
<td>2.1 (1.9–2.3)</td>
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</tr>
<tr>
<td></td>
<td>Femur/hip</td>
<td>6.0 (3.4–9.9)</td>
<td>3.3 (2.8–3.9)</td>
<td>2.7 (1.5–4.5)</td>
<td>2.7 (2.4–3.0)</td>
<td>2.8 (1.5–4.9)</td>
<td>1.8 (1.6–2.1)</td>
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<tr>
<td></td>
<td>Vertebral</td>
<td>4.0 (1.3–9.4)</td>
<td>2.2 (1.6–3.0)</td>
<td>1.9 (0.4–5.7)</td>
<td>1.6 (1.2–2.1)</td>
<td>1.6 (1.0–2.4)</td>
<td>1.6 (1.0–2.4)</td>
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</tr>
<tr>
<td>Femur/hip</td>
<td>Any fracture</td>
<td>8.1 (6.4–10.1)</td>
<td>3.9 (3.5–4.4)</td>
<td>4.3 (3.5–5.3)</td>
<td>3.1 (2.9–3.4)</td>
<td>2.8 (2.0–3.8)</td>
<td>2.1 (2.0–2.3)</td>
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<tr>
<td></td>
<td>Radius/ulna</td>
<td>10.0 (5.7–16.2)</td>
<td>2.5 (2.0–3.2)</td>
<td>4.3 (2.3–7.2)</td>
<td>2.8 (2.4–3.2)</td>
<td>1.1 (0.2–3.3)</td>
<td>1.6 (1.4–1.9)</td>
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<tr>
<td></td>
<td>Vertebral</td>
<td>11.4 (5.5–21.0)</td>
<td>3.8 (2.3–5.8)</td>
<td>3.3 (1.4–6.5)</td>
<td>2.5 (1.9–3.7)</td>
<td>2.7 (0.9–6.3)</td>
<td>1.7 (1.2–2.3)</td>
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<td></td>
</tr>
<tr>
<td>Vertebral</td>
<td>Any fracture</td>
<td>7.8 (5.8–10.3)</td>
<td>3.9 (3.4–4.6)</td>
<td>3.8 (2.7–5.3)</td>
<td>3.3 (2.9–3.7)</td>
<td>3.3 (2.0–5.2)</td>
<td>2.0 (1.7–2.4)</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Radius/ulna</td>
<td>4.2 (1.1–10.8)</td>
<td>1.9 (1.3–2.8)</td>
<td>3.3 (0.9–8.6)</td>
<td>2.1 (1.6–2.7)</td>
<td>1.4 (0.0–7.9)</td>
<td>0.9 (0.5–1.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Femur/hip</td>
<td>13.4 (7.3–22.5)</td>
<td>5.8 (4.1–8.1)</td>
<td>4.5 (2.4–7.5)</td>
<td>4.2 (3.5–4.9)</td>
<td>2.3 (0.8–5.0)</td>
<td>2.1 (1.6–2.7)</td>
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</tr>
</tbody>
</table>
Mortality rate related to number of vertebral fracture

Number of vertebral fractures

Mortality/1000 person-years

0 1 2 3 4 ≥5

p < 0.001

Kado DM. Arch Intern Med. 1999;159:1215-20
Mortality rate related to time after vertebral fracture

Incidence of vertebral fracture and subsequent mortality in South Korea, using nationwide data from the Health Insurance Review and Assessment from 2005 et 2008
This database covers 97% of Korean population
High number of patients with VF : 111 304 VF (2005) à 126 446 (2008)

Lee et al. OI 2012
Mortality after major fractures:
Hip, vertebrae, humerus, pelvis

Bliuc D et al, JAMA 2009

Women < 75 years-old

Women ≥ 75 years-old

Log-rank P < .001
No improvement in standardized mortality rate after major fractures over time

Dubbo Osteoporosis Epidemiology Study 1 (DOES 1; born before 1930): 1989 – 2004
Dubbo Osteoporosis Epidemiology Study 2 (DOES 2; born after 1930): 2000 – 2014
Hip Fracture Significantly Affects Quality of Life

- Functional decline was 32% at discharge and remained at 16% at 1 year.
- After 12 months, 30% of patients were still unable to walk independently compared to 7% of controls.
- 19% of patients were institutionalized over 1 year compared to 4% of controls.
- Mortality was 19% over 1 year compared to 3% in age and residence matched controls.

Excess Morbidity Caused by Fragility Fractures

- Hip fractures
- Fragility fractures: wrist, humerus, ankle, vertebrae
- Wrist fracture

Excess morbidity associated with fracture event
Morbidity attributable to ageing alone

www.capture-the-fracture.org
A Missed Opportunity to Prevent Secondary Fractures

- Half of patients presenting with hip fractures have suffered a prior fracture.

Wrist and vertebral fractures are common first fractures.
Orthogeriatric and FLS models effect on subsequent mortality post-hip fracture in UK

Forest plot of hazard ratios for outcomes within each hospital, comparing the time period after relative to the time period before orthogeriatric or FLS service model interventions. 33,152 primary hip fracture patients, 1,288 with a second hip fracture within 2 years (age and sex standardized ratio 4.2%)

Mortality within 30 days

Mortality within 1 year

Hawley S. Age and Ageing 2016; 45: 236–42
Capture the Fracture®

A global programme for the prevention of secondary fractures by facilitating the implementation of Fracture Liaison Services (FLS)

Capture the Fracture® name and logo are registered trademarks of IOF and should always be acknowledged with the trademark symbol.

www.capture-the-fracture.org
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Waterford Hospital, Ireland

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Prof. Stefan Goemaere
Ghent University Hospital, Belgium

Prof. Willem Lems
VU University medical centre, The Netherlands

CTF Steering Committee members

www.capture-the-fracture.org
Key Aims

- Be the global voice
- Drive national/international policy
- Ensure quality
- Provide support for FLS implementation, getting started & improving
234 FLS, 35 countries, 6 continents

- FLS in S. America = 17
- FLS in N. America = 36
- FLS in Europe = 142
- FLS in MENA region = 7
- FLS in APAC region = 32
Why join?

- Showcase your achievements
- Learn from the best practice framework to improve your service
- Get international recognition with a Gold, Silver, or Bronze star
- Be part of a global initiative to prevent secondary fractures

Who can participate?

- Coordinator-based models of care
- All type of facilities
- At any stage in development
- Any size worldwide
Purpose of the Best Practice Framework

Aim:
1. Set the standard for FLS
2. Guidance
3. Benchmarking and fine-tuning

5 domains, 13 standards
- Hip fracture patients
- Inpatient
- Outpatient
- Vertebral fracture patient
- Organization

Studies have shown that Fracture Liaison Service models are the most cost-effective in preventing secondary fractures. This systematic approach, with a fracture coordinator at its centre, can result in fewer fractures, cost savings for the health system and improvement in the quality of life of patients.

www.capture-the-fracture.org
13 BPF Criteria and Standards

<table>
<thead>
<tr>
<th>Standard</th>
<th>Bronze</th>
<th>Silver</th>
<th>Gold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Identification</td>
<td>Patients identified, <em>not</em> tracked</td>
<td>Patients identified, <em>are</em> tracked</td>
<td>Patients identified, tracked &amp; independently reviewed</td>
</tr>
</tbody>
</table>

**Standard 1 definition:**
Fracture patients are identified to enable delivery of secondary fracture prevention.
# BPF Criteria and Standards

**Standard 2 definition:**
Identified patients are assessed for future fracture risk

<table>
<thead>
<tr>
<th>Standard</th>
<th>Bronze</th>
<th>Silver</th>
<th>Gold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Evaluation</td>
<td>50% are assessed</td>
<td>70% are assessed</td>
<td>90% are assessed</td>
</tr>
</tbody>
</table>

**Standard 3 definition:**
Post-fracture assessment is conducted in a timely fashion after clinical fracture presentation

<table>
<thead>
<tr>
<th>Standard</th>
<th>Bronze</th>
<th>Silver</th>
<th>Gold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post Fracture Assessment</td>
<td>Within 13-16 weeks</td>
<td>Within 9-12 weeks</td>
<td>Within 8 weeks</td>
</tr>
<tr>
<td>Assessment Timing</td>
<td></td>
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</tr>
</tbody>
</table>

www.capture-the-fracture.org
### BPF Criteria and Standards

**Standard 4** definition:
System to identify vertebral fractures

<table>
<thead>
<tr>
<th>Standard</th>
<th>Bronze</th>
<th>Silver</th>
<th>Gold</th>
</tr>
</thead>
<tbody>
<tr>
<td>VF id</td>
<td>Known VF identified</td>
<td>Routinely identified for VF</td>
<td>Radiologists identify VF</td>
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</tbody>
</table>

**Standard 5** definition:
Secondary fracture prevention assessment is consistent with guidelines

<table>
<thead>
<tr>
<th>Standard</th>
<th>Bronze</th>
<th>Silver</th>
<th>Gold</th>
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</thead>
<tbody>
<tr>
<td>Assessment Guidance</td>
<td>Local</td>
<td>Regional</td>
<td>National</td>
</tr>
</tbody>
</table>
The optimal fracture liaison service (FLS)

Emergency Room
All patients > 50 with clinical fracture

Orthopedic department

Inpatient visits

Database

Radiology department
All patients > 50 with VF on any imaging

Daily Identification of patients

Home or Rehabilitation

Phone calls

Risk of falls assessment and prevention

Information and coordination with GP

Treatment initiation & Follow up

Bone specialist visit

DXA
The fracture cascade is a clinical reality

When a first fracture occurs, the risk of recurrence is maximal in the next first months

The first fracture should be the last one
  - Appropriate measures
  - Pharmacological treatments have to be considered when the risk is high

FLS is a model of cost-effective management
Q&A session
Thanks to our CTF sponsors

Inspired by patients.
Driven by science.
Acknowledgements

On behalf of IOF and the CTF steering committee, we thank you for your participation in this webinar.

If you have any additional questions, comments or feedback please email capturethefracture@iofbonehealth.org