Obesity and Bone

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Disclosures

	Speaker	Advisory	Research
Amgen	√		
Ascendis Pharma			√
Eli Lilly	√		
Novo Nordisk		√	√
Shire/Takeda			√

CanMEDS Roles Covered: GAGNON - “Canadian Obesity Weekend 2022”

X	**Medical Expert** (as *Medical Experts*, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. *Medical Expert* is the central physician Role in the CanMEDS Framework and defines the physician’s clinical scope of practice.)
	Communicator (as Communicators, physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)
	Collaborator (as *Collaborators*, physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)
	Leader (as *Leaders*, physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)
X	**Health Advocate** (as *Health Advocates*, physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)
X	**Scholar** (as *Scholars*, physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)
	Professional (as *Professionals,* physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)

Learning Objectives

1. To **contrast fracture risk** in people with vs without obesity
2. To **discuss** briefly the **pathophysiology** of bone fragility and **risk factors** for fracture in people with obesity
3. To **summarize** the **prevention** and **treatment** of fractures in obesity

CLINICAL CASE

Clinical Case

- 58 year-old postmenopausal woman
- BMI of 38 kg/m^2
- Ankle fracture last summer while walking on uneven ground
- Normal bone mineral density (BMD)

Lermagazine.com

FRACTURE RISK IN PEOPLE LIVING WITH OBESITY

PLOS ONE

RESEARCH ARTICLE

Association between obesity and risk of fracture, bone mineral density and bone quality in adults: A systematic review and meta-analysis

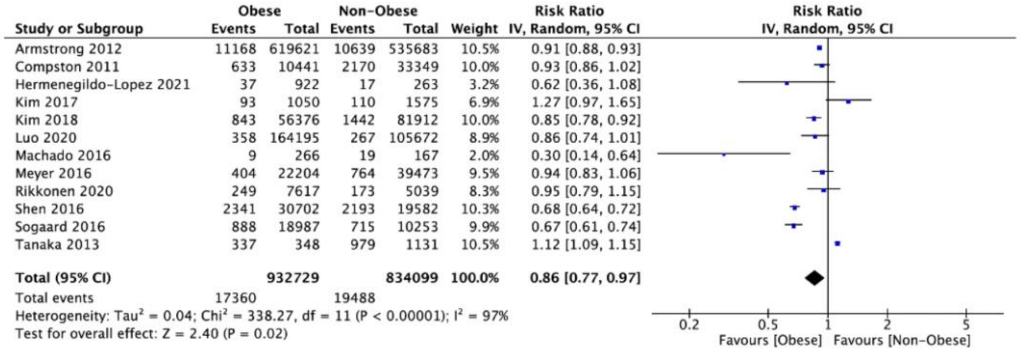
Anne-Frédérique Turcotte[1,2,3], Sarah O'Connor[4,5,6], Suzanne N. Morin[7], Jenna C. Gibbs[8], Bettina M. Willie[9], Sonia Jean[3,6], Claudia Gagnon[1,2,3]*

Published in June 2021

Obesity and Risk of Fracture at Any Skeletal Site

MENOPAUSE

n=12



Study or Subgroup	Obese Events	Obese Total	Non-Obese Events	Non-Obese Total	Weight	Risk Ratio IV, Random, 95% CI
Armstrong 2012	11168	619621	10639	535683	10.5%	0.91 [0.88, 0.93]
Compston 2011	633	10441	2170	33349	10.0%	0.93 [0.86, 1.02]
Hermenegildo-Lopez 2021	37	922	17	263	3.2%	0.62 [0.36, 1.08]
Kim 2017	93	1050	110	1575	6.9%	1.27 [0.97, 1.65]
Kim 2018	843	56376	1442	81912	10.0%	0.85 [0.78, 0.92]
Luo 2020	358	164195	267	105672	8.9%	0.86 [0.74, 1.01]
Machado 2016	9	266	19	167	2.0%	0.30 [0.14, 0.64]
Meyer 2016	404	22204	764	39473	9.5%	0.94 [0.83, 1.06]
Rikkonen 2020	249	7617	173	5039	8.3%	0.95 [0.79, 1.15]
Shen 2016	2341	30702	2193	19582	10.3%	0.68 [0.64, 0.72]
Sogaard 2016	888	18987	715	10253	9.9%	0.67 [0.61, 0.74]
Tanaka 2013	337	348	979	1131	10.5%	1.12 [1.09, 1.15]
Total (95% CI)		**932729**		**834099**	**100.0%**	**0.86 [0.77, 0.97]**
Total events	17360		19488			

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 338.27$, df = 11 ($P < 0.00001$); $I^2 = 97\%$

Test for overall effect: $Z = 2.40$ ($P = 0.02$)

Risk Ratio IV, Random, 95% CI

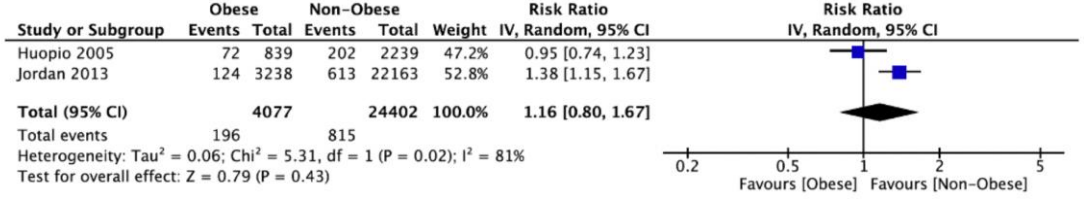
0.2 0.5 1 2 5

Favours [Obese] Favours [Non-Obese]

14%

0.86 (0.77-0.97); I^2=97%

n=2



Study or Subgroup	Obese Events	Obese Total	Non-Obese Events	Non-Obese Total	Weight	Risk Ratio IV, Random, 95% CI
Huopio 2005	72	839	202	2239	47.2%	0.95 [0.74, 1.23]
Jordan 2013	124	3238	613	22163	52.8%	1.38 [1.15, 1.67]
Total (95% CI)		**4077**		**24402**	**100.0%**	**1.16 [0.80, 1.67]**
Total events	196		815			

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 5.31$, df = 1 ($P = 0.02$); $I^2 = 81\%$

Test for overall effect: $Z = 0.79$ ($P = 0.43$)

Risk Ratio IV, Random, 95% CI

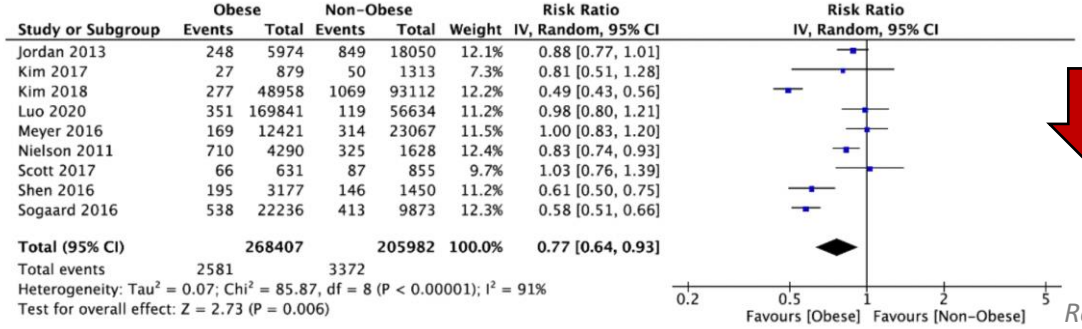
0.2 0.5 1 2 5

Favours [Obese] Favours [Non-Obese]

Non conclusive

1.16 (0.80-1.67); I^2=81%

n=9



Study or Subgroup	Obese Events	Obese Total	Non-Obese Events	Non-Obese Total	Weight	Risk Ratio IV, Random, 95% CI
Jordan 2013	248	5974	849	18050	12.1%	0.88 [0.77, 1.01]
Kim 2017	27	879	50	1313	7.3%	0.81 [0.51, 1.28]
Kim 2018	277	48958	1069	93112	12.2%	0.49 [0.43, 0.56]
Luo 2020	351	169841	119	56634	11.2%	0.98 [0.80, 1.21]
Meyer 2016	169	12421	314	23067	11.5%	1.00 [0.83, 1.20]
Nielson 2011	710	4290	325	1628	12.4%	0.83 [0.74, 0.93]
Scott 2017	66	631	87	855	9.7%	1.03 [0.76, 1.39]
Shen 2016	195	3177	146	1450	11.2%	0.61 [0.50, 0.75]
Sogaard 2016	538	22236	413	9873	12.3%	0.58 [0.51, 0.66]
Total (95% CI)		**268407**		**205982**	**100.0%**	**0.77 [0.64, 0.93]**
Total events	2581		3372			

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 85.87$, df = 8 ($P < 0.00001$); $I^2 = 91\%$

Test for overall effect: $Z = 2.73$ ($P = 0.006$)

Risk Ratio IV, Random, 95% CI

0.2 0.5 1 2 5

Favours [Obese] Favours [Non-Obese]

23%

0.77 (0.64-0.93); I^2=91%

Results are presented in RR (95% CI).

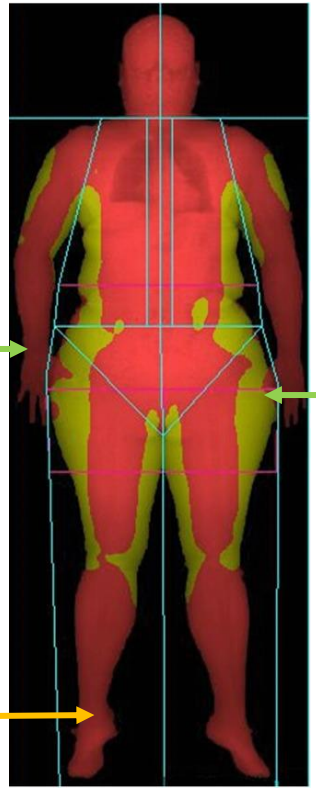
Fracture Risk Differs by Skeletal Site in Obesity

MENOPAUSE

n=2

15%

0.85 (0.81-0.88); I^2=0%



MENOPAUSE

n=8

25%

0.25 (0.62-0.91); I^2=95%

♂

n=5

41%

0.59 (0.44-0.79); I^2=91%

MENOPAUSE

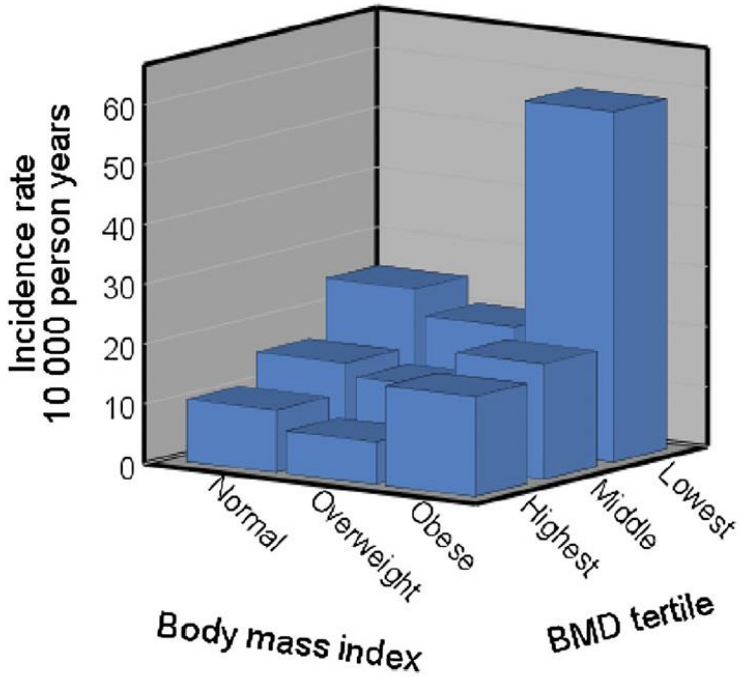
n=2

60%

1.60 (1.52-1.68); I^2=0%

Results are presented in RR (95% CI).

Hip Fracture Risk and Obesity: A complex Relationship



Postmenopausal women with obesity have a higher risk of hip fracture before age 70, especially if BMD is lower

Rikkonen. *Osteoporosis Int*, 2021.

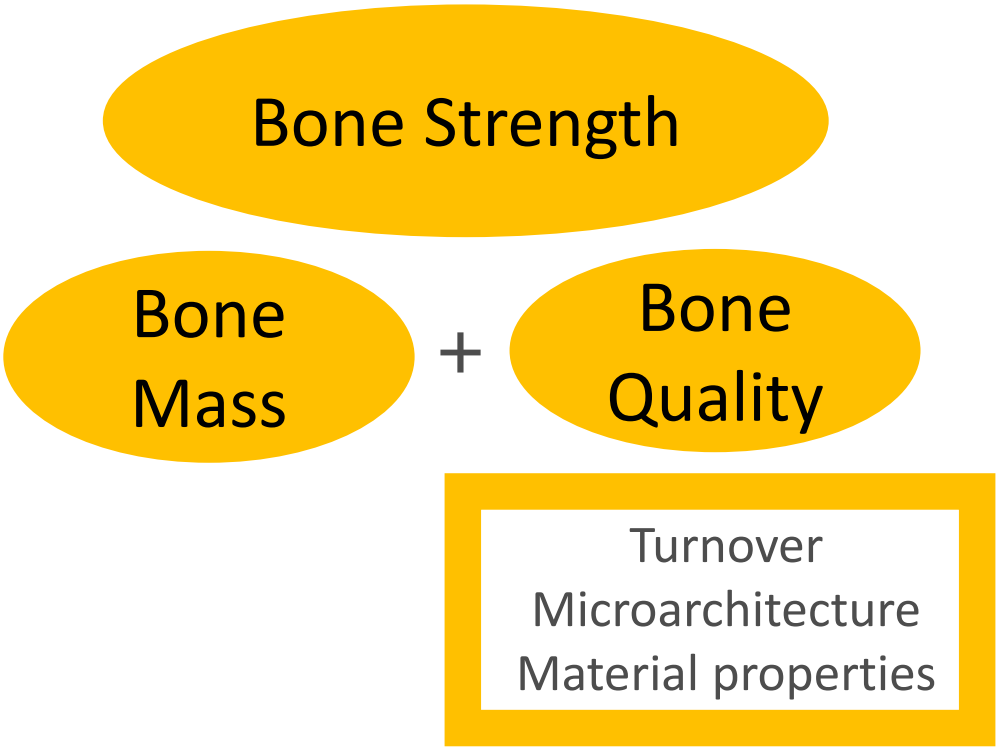
Fracture Risk Differs based on the Definition of Obesity

- **General Obesity (BMI)**
  - **Lower risk of wrist** fractures[1]
  - Controversial results for **hip** fracture risk[1,2]
  - Increased risk of **ankle**[1] and **upper arm**[3] fractures
- **Abdominal Obesity (WC)**
  - **Increased risk of hip** fracture (meta-analysis)[4]
  - **Increased risk of femur** and **vertebral** fractures[5]
  - Linear increase in the risk of **lower limb** fractures[6]

[1]Turcotte AF. *Plos One*, 2021; [2]Rikkonen. *OI*, 2021; [3]Johansson. *J Bone Miner Res*, 2014; [4]Sadeghi. *Adv Nutr*, 2017; [5]Park. *Eur Rev Med Pharmacol Sci*, 2021; [6]Turcotte AF. *Abstract IFSO/EASO*, May 2022.

PATHOPHYSIOLOGY AND RISK FACTORS FOR FRACTURE IN OBESITY

Fracture Risk Depends on Skeletal Factors



General obesity (BMI)[1]

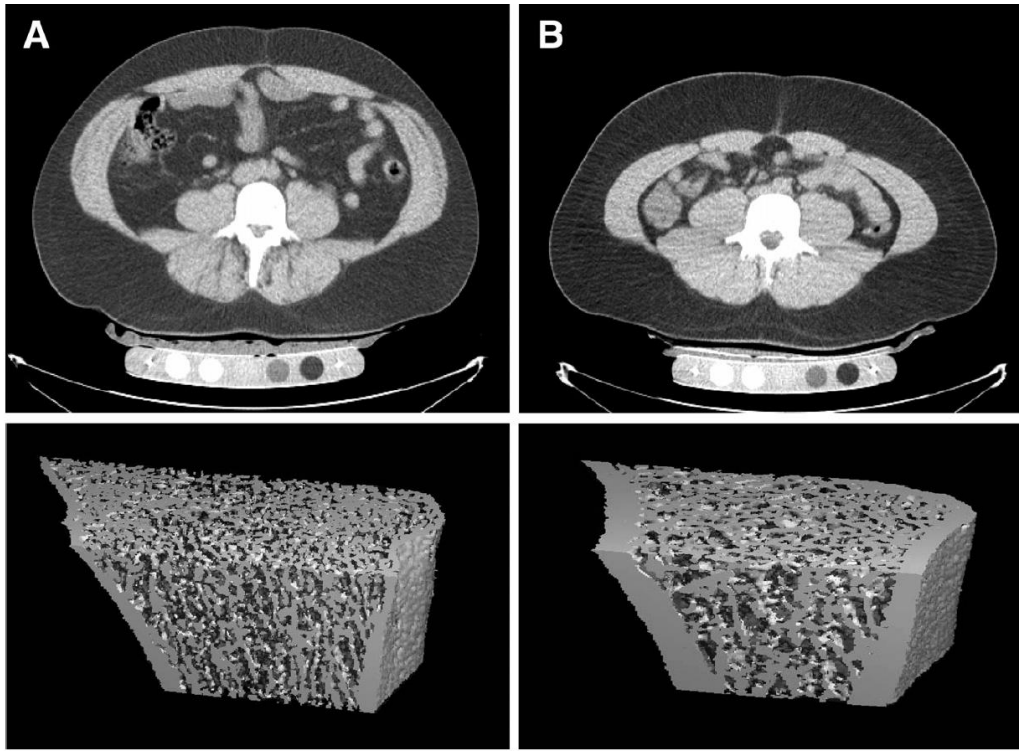
- Bone mass similar/higher
- Favorable bone microarchitecture (few data)
- Lower bone resorption and variable formation markers

Abdominal obesity (WC)[2,3]

- Bone mass lower
- Unfavorable bone microarchitecture
- Lower bone formation[4]

[1]Turcotte AF. *Plos One*, 2021; [2]Bredella. *JCEM*, 2016; [3]Bredella. *Bone*, 2011; [4]Cohen A. *JCEM*. 2013.

Abdominal Obesity is Detrimental for Bone Health



BMI 32 + high VAT **BMI 32 + low VAT**

1. Low-grade inflammation (-)
2. Bone marrow adiposity (-)
3. Hormones (+/-)
4. Vitamin D deficiency (-)
5. Muscle (+)

Bredella M. *JCEM*, 2016.

Fracture Risk Depends Also on Clinical Risk Factors

Clinical Risk Factors

Not specific to Obesity: Age, menopause, …

Enhanced by Obesity: Falls, diabetes/other comorbidities, vitamin D/nutrient deficiencies

Multifactorial Increase in Falls Risk in People Living with Obesity

CAUSES FOR INCREASED RISK

⇩ agility
Postural instability
Poor physical activity → ⇩ strength and agility
Fatty infiltration of the muscles → Dynapenic obesity
Comorbidities → Neurological impairment
Osteoarthritis → Difficult walk

HYPOTHESES FOR PARADOXICAL FRACTURE SITE DISTRIBUTION

Hip padding (protective)
Backward or sideward falling
Introversion and extroversion of the ankle and lower leg → Sprains and fractures of the ankle

Rinonapoli G. *Inter J Molec Sci*, 2021; Himes CL, *JAGS*, 2011.

Diabetes impairs bone quality

SEASON 2, EPISODE 5

DIABETES AND OSTEOPOROSIS WITH DR. CLAUDIA GAGNON

ORIGINAL AIR DATE: JUNE 2, 2021

Dr. Claudia Gagnon is an Associate Professor in the Department of Medicine at Université Laval and a clinician-researcher scholar of the Fonds de recherche en santé du Québec. She is also active as a member of the Osteoporosis Canada (OC) Scientific Advisory Council. Dr. Gagnon's research focuses on the impact of obesity, diabetes and their treatments (in particular bariatric surgery) on bone health. In this podcast she discusses why both men and women with diabetes are at higher risk for low bone density and for osteoporotic fractures.

Play Episode

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PREVENTION AND TREATMENT OF FRACTURES IN OBESITY

Recommendations are the Same as for People Without Obesity

Calcium, vitamin D, protein
Stop smoking, reduce alcohol

Weight-bearing
and balance exercises

Fall prevention
strategies

If Diabetes: reduce hypoglycemia and optimize diabetes control

Review medication list and start anti-osteoporosis drugs if required

BACK TO THE CLINICAL CASE

Fracture Prevention Strategies

Based on fracture risk calculation (FRAX):
No indication for anti-osteoporosis drugs
but ensure adequate calcium,
vitamin D and nutrients

r/o secondary causes
of osteoporosis

Weight-bearing and
balance exercises

Fall prevention
strategies

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Conclusions

1. People living with obesity have a higher risk of fracture at certain skeletal sites that varies by definition of obesity
2. Pathophysiology and risk factors are unclear but
   - Falls risk, fat distribution and concomitant comorbidities are likely involved
   - Those with a low BMD/bone quality may be especially at risk

Thank you!

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