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Fractures in indigenous compared to non-indigenous populations: A systematic review of rates and aetiology

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ABSTRACT

Background: Compared to non-indigenous populations, indigenous populations experience disproportionately greater morbidity, and a reduced life expectancy; however, conflicting data exist regarding whether a higher risk of fracture is experienced by either population. We systematically evaluate evidence for whether differences in fracture rates at any skeletal site exist between indigenous and non-indigenous populations of any age, and to identify potential risk factors that might explain these differences.

Methods: On 31 August 2016 we conducted a comprehensive computer-aided search of peer-reviewed literature without date limits. We searched PubMed, OVID, MEDLINE, CINAHL, EMBASE, and reference lists of relevant publications. The protocol for this systematic review is registered in PROSPERO, the International Prospective Register of systematic reviews (CRD42016043215). Using the World Health Organization reference population as standard, hip fracture incidence rates were re-standardized for comparability between countries.

Results: Our search yielded 3227 articles; 283 potentially eligible articles were cross-referenced against predetermined criteria, leaving 27 articles for final inclusion. Differences in hip fracture rates appeared as continent-specific, with lower rates observed for indigenous persons in all countries except for Canada and Australia where the opposite was observed. Indigenous persons consistently had higher rates of trauma-related fractures; the highest were observed in Australia where craniofacial fracture rates were 22-times greater for indigenous compared to non-indigenous women. After adjustment for socio-demographic and clinical risk factors, approximately a three-fold greater risk of osteoporotic fracture and five-fold greater risk of craniofacial fractures was observed for indigenous compared to non-indigenous persons; diabetes, substance abuse, comorbidity, lower income, locality, and fracture history were independently associated with an increased risk of fracture.

Conclusions: The observed paucity of data and suggestion of continent-specific differences indicate an urgent need for further research regarding indigenous status and fracture epidemiology and aetiology. Our findings also have implications for communities, governments and healthcare professionals to enhance the prevention of trauma-related fractures in indigenous persons, and an increased focus on modifiable lifestyle behaviours to prevent osteoporotic fractures in all populations.

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1. Introduction

Indigenous compared to non-indigenous persons experience disproportionately greater morbidity and reduced life expectancy (Cooke et al., 2007); there has been concerted effort to close this gap over recent years (Brennan-Olsen et al., 2016).

Specific to musculoskeletal health, some data suggest that indigenous persons have a higher risk of sustaining a fracture compared to non-indigenous peoples (Leslie et al., 2005), whilst other studies report no differences in fracture rates between the two groups (Cauley et al., 2007); these differences in rates may potentially vary according to skeletal site, and correlate with cause of fracture (Karmali et al., 2005; Cauley, 2011). It is also unknown whether any differences in fracture rates between indigenous and non-indigenous populations may vary between countries, or with the prevalence of specific risk factors. These conflicting associations and poorly understood risk factors create an imperative to investigate incident fracture rates at different skeletal sites for indigenous compared to non-indigenous populations, and to identify factors that could explain any differences in fracture rates, and thus form the aims of this systematic review.

2. Methods

The protocol for this systematic review has been published (Brennan-Olsen et al., 2016) and is registered with the International Prospective Register of systematic reviews (registration number CRD42016043215); as such, it adheres to the preferred reporting processes outlined within the Preferred Reporting Items for Systematic reviews and Meta-Analyses Protocols (PRISMA-P) 2015 guidelines (Moher et al., 2015).

2.1. Indigenous status

Our inclusion criteria regarding indigenous status for eligible studies aligns with Article 33 of the *United Nations Declaration on the Rights of Indigenous Peoples*, whereby the importance of self-identification as an indigenous person is ranked highly (United Nations, 2007). We also included papers that determined indigenous status according to country-specific identity registration systems, or by parent-report.

2.2. Criteria for considering studies for this review

Inclusion criteria for eligible studies are: published full-text articles (epidemiological cohort, case-control and/or cross-sectional studies) that examine fracture rates, present proportions of fractures, and/or present multivariable models for the risk of fracture in indigenous populations or for indigenous compared to non-indigenous populations. Eligibility criteria for studies are inclusive of any country, sex or age. We included studies that ascertained fracture by self-report, radiological reports, clinical diagnosis, hospital or clinic admission, and/or according to the International Statistical Classification of Disease (ICD) codes from hospitalization or administrative health records.

Grey literature, conference presentations, theses and letters were excluded. Given that the purpose of this review is to ascertain whether fracture rates differ between non-indigenous and indigenous populations, randomized controlled trials (RCTs) were also excluded. If relevant, however, and where possible, baseline data from RCTs that pertain to fracture rates prior to intervention were included. Finally, papers that investigated both indigenous and non-indigenous persons but did not present findings separately for each group were excluded.

2.3. Search strategy for identification of studies

Our computer-generated search strategy was performed using PubMed, OVID, MEDLINE, CINAHL and EMBASE to identify relevant literature; the search was performed on 31st August 2016, and no limits on the date of publication were set. The following medical subject headings (MeSH) were applied: 'osteoporosis' OR 'fractures' OR 'bone' AND ('Indigenous' OR 'Aborigines' OR 'Inuit' OR 'Indians, Central American' OR 'Indians, North American' OR 'Indians, South American' OR 'Oceanic Ancestry Group'). Key words (informed by the United Nations Permanent Forum on Indigenous Issues (United Nations, 2007)) included: aboriginal, Aleutians, American Indian, First Nation, Lakota, Maasai, Maori, Mayas, Métis, Native Americans, Native-born,

Saami, Torres Strait Islander and indigenous peoples. Relevant truncation was used for each database.

2.4. Re-standardization

Given that age is a major confounder for fractures, and each study identified had used a different age range, the reported rates of fractures could not be compared between studies without standardization (Tripepi et al., 2010). Thus, whilst re-standardization of hip fractures was not an a priori element of our planned analyses, it was performed to address the differences in age ranges between studies, and in order to aid the comparison of rates between countries. Due to few data pertaining to other skeletal sites, we only re-standardized hip fractures. Reported crude rates of hip fractures across specific age-groups (including 95% confidence intervals), number of fractures and person-years observed for those aged ≥65 years were extracted either from the tables or digitised from published figures. The crude hip fracture rates were re-standardized using the direct standardization method and with World Health Organization (WHO) standard population (WHO 2000–2025) as a reference. When only sex-specific crude rates were provided in the published article, the re-standardization of the overall sample was not possible, and vice versa. Meta-analyses were not attempted due to cultural governance determining much heterogeneity between indigenous populations from different continents.

3. Results

3.1. Identification and selection of the literature

Table 1 presents a summary of the literature identification and selection. Our computer-assisted search strategy yielded 3227 articles, of which 708 were potentially eligible. After screening, 283 articles remained as potentially eligible; the full-texts of those articles were read and cross-referencing against our pre-determined criteria, and 262 full text articles were excluded, leaving 21 articles that met our selection criteria (Leslie et al., 2004, 2005, 2006, 2012, 2013; Cauley et al., 2007, 2011; Adsett et al., 2013; Buchanan et al., 2005; Chen et al., 2010; Frech et al., 2012; Jandoc et al., 2015; Kieser et al., 2002; Kruger et al., 2006; MacIntosh and Pearson, 2001; MacMillan et al., 2010; Oberdan and Finn, 2007; Pratt and Holloway, 2001; Stott et al., 1980; Wong et al., 2013; Nelson et al., 2011). The most frequent reasons for articles failing to meet the eligibility criteria at this stage of the identification process were: archeological investigations of skeletons (n = 91); studies investigated bone mineral density (BMD); bone mineral content (BMC) or body composition (n = 50); study populations investigated with regards to ethnicity not indigenous status (n = 37); or dental-based studies (n = 31); with the remaining 53 articles excluded for other reasons (Table 1). The reference lists of the 21 eligible articles were hand-searched, from which a further 6 articles were identified as eligible for inclusion (Barber et al., 1995; Barrett-Connor et al., 2005; Orchard et al., 2013; Norton et al., 1995; Koorey et al., 1992; Beyene and Martin, 2001), resulting in a total of 27 papers to be reviewed. A quality-control check was performed by SEQ of a randomly-selected sample (using electronically generated random numbers) of ~10% of the 262 excluded full-text articles (n = 25), and by SEQ and BJD of an electronically-generated random sample of ~50% of the included full-text articles (n = 15): with the exception of one paper determined to be ineligible due to fracture cases defined as 'prevalent osteoporosis' being grouped with non-fracture morbidity (Martens et al., 2011), authors agreed on all of the excluded and included articles examined for quality control.

Table 1
Summary of article identification from the electronic search of databases; reasons for exclusion are presented in order of the most common to the least common.

Database sources:		PubMed OVID Medline CINAHL EMBASE
	Excluded n=	Reason for exclusion
Identified 3227 citations	2351	Not relevant
	168	Duplicates
	(n = 2519)	
Reviewed 708 titles and abstracts	138	Dental
	91	Other diseases
	51	Conference abstracts
	48	Animal studies
	36	Diet or nutritional intake
	32	Medication or treatment
	24	Anthropological
	4	Vitamin D
	1	Review
	(n = 425)	
Reviewed 283 complete articles	91	Archeological studies
	50	BMD/BMC/body composition
	37	Ethnicity not indigenous
	31	Dental
	15	Medication or treatment
	14	Other diseases
	10	Diet or nutritional intake
	8	Animal studies
	2	Review
	1	Indigenous and non-indigenous combined
	1	Pain
	1	Vitamin D; exposure or metabolism
	1	Letter
	(n = 262)	
Subtotal: articles determined as eligible for inclusion	21	
Eligible articles identified from reference list search	6	
Total: articles eligible for inclusion	27	

3.2. Description of the studies

Table 2 presents an overview of the 27 included articles. The articles were published across four decades from 1980 to 2015. Combined, the studies encompassed analyses of approximately 123,000 indigenous persons; however, both the Women's Health Initiative dataset from the USA and the Province wide Manitoba administrative health database from Canada investigated in more than one study. Studies were performed in New Zealand (n = 7) (Adsett et al., 2013; Buchanan et al., 2005; Kieser et al., 2002; Stott et al., 1980; Barber et al., 1995; Norton et al., 1995; Koorey et al., 1992), the United States of America (USA) (n = 7) (Cauley et al., 2007, 2011; Chen et al., 2010; Frech et al., 2012; Pratt and Holloway, 2001; Nelson et al., 2011; Barrett-Connor et al., 2005), Canada (n = 7) (Leslie et al., 2004, 2005, 2006, 2012, 2013; Jandoc et al., 2015; MacMillan et al., 2010), Australia (n = 5) (Kruger et al., 2006; MacIntosh and Pearson, 2001; Oberdan and Finn, 2007; Wong et al., 2013; Orchard et al., 2013) and Mexico (n = 1) (Beyene and Martin, 2001). Standardized, age-adjusted and/or annualized incident fracture rates or ratios were presented within 14 of the 27 articles, multivariable analyses were presented within 5 of the included articles, and 12 of the articles presented only descriptive results or had presented adjusted analyses that were not relevant to this systematic review; for instance time to mortality post-fracture for indigenous compared to non-indigenous persons (Leslie et al., 2013), the number of football games missed following fracture for indigenous compared to non-indigenous players (Orchard et al., 2013), the role played by parathyroid hormone (Cauley et al., 2011) or anemia status (Chen et al., 2010) on fracture risk within a group of indigenous persons, or the post-fracture care-gap among indigenous compared to non-indigenous populations (Leslie et al., 2012).

Table 2
Characteristics of the reviewed studies, presented alphabetically by country, and in reverse chronological order according to year of publication.

Author et al, year of publication	Study subjects (% women)	Age, presented as years, or mean (±SD)	Study period	Study design and population description	Skeletal fracture site (total fractures in sample; % sustained by Indigenous persons)	Fracture ascertainment, incl. ICD-9/10 codes where provided	Fracture cause, incl. ICD-9/10 codes where provided	Type of results: IR, MR, DO
Australia								
Orchard, 2013 [31]	Indigenous: 182 (0%) Non-Indigenous: 4,310 (0%)	23.6 (±3.6)	1992–2012	Retrospective cross-sectional study; AFL players identified from annual AFL injury surveys conducted Australia wide	Facial: (209; [a]) Clavicle: (99; [a]) Forearm/wrist/hand: (448; [a]) Leg/foot: (247; [a]) Leg/foot (stress): (345; [a])	Players' injury records database	Sports-related	DO
Wong, 2013 [27]	Indigenous: 201 (54.2%) Non-Indigenous: 11,643 (74.8%)	≥40	1999–2009	Age-standardized incidence rates over 10 years using the 2006 population from the Australian Bureau of Statistics as standard; cases retrospectively identified from the Western Australia HMDS, which included all public and private hospital admissions in the state	Hip: (11,844; 1.7%)	Hospital admissions; ICD-10 codes (Australian modification) S72.0, S72.1, S72.2	External causes related to minimal trauma (ICD-10 codes W00, W01, W03-08, W18-19, W22, W50-51, W54.8)	IR
Kruger, 2006 [17]	Indigenous: 681 (33.5%) Non-Indigenous: 1,922 (14.7%)	0+	1999–2000 2002–2003	Age-specific and age-standardized rates over 4 years using population estimates calculated by the Health Department of Western Australia as derived from census data collected by the Australian Bureau of Statistics; cases identified from the Western Australia HMDS, which included all public and private hospital admissions in the state	Mandibular: (1,611; [a]) Maxillary: (992; [a]) Total: (2,603; 26.2%)	Hospital admissions; ICD-10 codes S02.4-S02.6	[a]	IR
Oberdan, 2007 [24]	Indigenous: 134 (23.9%) Non-Indigenous: 142 (14.8%)	0+	1999–2002	Retrospective cross-sectional descriptive study; cases presenting to the Cairns Base Hospital, Queensland, Australia	Mandibular: (444; 49%)	Hospital records; ICD-9 codes 802.0-803.4 or ICD-10 codes S02.3-S02.9	Assault, road traffic accident, sport, fall, other	DO
Macintosh, 2001 [22]	Indigenous: 15 (60.0%) Non-Indigenous: 213 ([a, b])	0+	1997–2000	Retrospective cross-sectional descriptive study; cases admitted to Cairns Base Hospital, Queensland, Australia; data gathered from 'Clinical Pathways' hospital database	Hip (femoral neck): (232; 6.5%)	'Clinical diagnosis'	[a]	DO
Canada								
Jandoc, 2015 [15]	Indigenous (Metis only): 4,219 (45%) Non-Indigenous: 2,198,661 (91.8%)	≥50	2006–2011	Sex-stratified and age-standardized rates using direct standardization using the 1991 Ontario, Canada, census population as the standard; cases retrospectively	Hip: (49,375; 0.06%) Humerus: (41,382; 0.08%) Radius/ulna: (84,334; 0.10%)	[a]	[a]	IR, MR

Table 2 (*continued*)

Author et al, year of publication	Study subjects (% women)	Age, presented as years, or mean (±SD)	Study period	Study design and population description	Skeletal fracture site (total fractures in sample; % sustained by Indigenous persons)	Fracture ascertainment, incl. ICD-9/10 codes where provided	Fracture cause, incl. ICD-9/10 codes where provided	Type of results: IR, MR, DO
				identified over 5 years from Province wide (Ontario) administrative health database				
Leslie, 2013 [20]	Non-Indigenous: 39,866 ([a])	≥50	*Population 1* 1996–2004 *Population 2* 1987–2002	Retrospective case-control study; Province wide (Manitoba) administrative health database	*Population 1* Hip: (4,145; 4.1%) Wrist: (8,216; 5.3%) Vertebral: (3,431; 3.1%) *Population 2* Hip: (41,211; 3%)	ICD-9 (Clinical modification) fracture codes involving the hip (with site-specific fixation code), forearm (with site-specific fracture fixation or casting code), or clinical spine (without cord injury)	Low trauma (external causes related to high-trauma injuries, according to 'E' codes, excluded)	DO
Leslie, 2012 [19]	Indigenous: 502 ([a]) Non-Indigenous: 10,732 ([a])	≥50	1996–2002	Retrospective cohort study; Province wide (Manitoba) administrative health database	Hip: (3,058; [a]) Wrist: (5,760; [a]) Vertebral: (2,146; [a]) Combined: (11,234; 4.5%)	ICD-9 (Clinical modification) fracture codes involving the hip (with site-specific fixation code), forearm (with site-specific fracture fixation or casting code), or clinical spine (without cord injury)	Low trauma; external causes related to high-trauma injuries, according to 'E' codes were excluded	DO
MacMillan, 2010 [23]	Indigenous: 3,791 (49%) Non-Indigenous:	Indigenous: 8.7 (±5.0) Non-indigenous: 5.5 (±3.4)	1996–1997	Retrospective cross-sectional descriptive study; 'On-reserve' child and youth participants in the FNIRHS (combines data from 9 regional surveys conducted in Aboriginal reserve communities in all Canadian provinces)	[a]	Parent-reported by questionnaire	[a]	DO
Leslie, 2006 [21]	Indigenous: 27,952 (52.2%) Non-Indigenous: 83,856 (52.2%)	≥20	1984–2003	Retrospective population-based matched cohort study; Province wide (Manitoba) administrative health database	Hip: (767; 39.6%) Wrist: (750; 49.5%) Vertebral: (1,210; 37.1%) Craniofacial: (2,303; 62%)	ICD-9 (Clinical modification) fracture codes at any site 800-829, codes for hip fracture included reduction or fixation 820-821, wrist with fracture reduction or fixation 813, spine without cord injury 805, craniofacial 800-804	Osteoporosis-related (hip, wrist, vertebrae), trauma-related (craniofacial)	IR, MR
Leslie, 2005 [3]	Indigenous: 31,557 (50.5%) Non-Indigenous: 79,720 (50.8%)	≥20	1987–1999	Retrospective population-based matched cohort study with standardized incidence ratios; Province wide (Manitoba) administrative health database	Hip: (708; 44.8%) Wrist: (950; 50.9%) Vertebral: (1,474; 41%) Craniofacial: (3,703; 62%) Any site: (24,529; 43.8%)	ICD-9 (Clinical modification) fracture codes at any site 800-829 (specific analyses used codes for hip including fracture reduction or fixation 820-821, wrist with fracture reduction or fixation 813, spine without cord injury 805, craniofacial 800-804)	Osteoporosis-related (hip, wrist, vertebrae), trauma-related (craniofacial)	MR
Leslie, 2004 [18]	Indigenous: 32,692 (50.8%) Non-Indigenous: 98,076 (50.8%)	≥20	1987–1999	Retrospective matched-cohort study with standardized incidence ratios; Province wide (Manitoba) administrative health database	Hip: (876; 36.8%) Wrist: (989, 50.3%) Vertebral: (1,551; 39.9%) Craniofacial: (3,805; 63.3%) Any site: (27,370: 40.6%)	ICD-9 (Clinical modification) fracture codes at any site 800-829 (specific analyses used codes for hip including fracture reduction or fixation 820-821, wrist with fracture	Osteoporosis-related (hip, wrist, vertebrae), trauma-related (craniofacial)	IR

(*continued on next page*)

Table 2 (*continued*)

Author et al, year of publication	Study subjects (% women)	Age, presented as years, or mean (±SD)	Study period	Study design and population description	Skeletal fracture site (total fractures in sample; % sustained by Indigenous persons)	Fracture ascertainment, incl. ICD-9/10 codes where provided	Fracture cause, incl. ICD-9/10 codes where provided	Type of results: IR, MR, DO
						reduction or fixation 813, spine without cord injury 805, craniofacial 800-804)		
Mexico								
Beyene, 2001 [34]	*Population 1:* Indigenous: 228 (100%) Non-indigenous: – *Population 2:* Indigenous: 456 (<1%) Non-indigenous: 629 ([a])	Pre-menopausal: 33.3 (±9.0) Post-menopausal: 56.6 (±10.5)	[a]	*Population 1:* Cross-sectional, convenience sample from Chichimila (rural village with population of ~3,000) and/or Valladolid (an adjacent colonial town with a population of ~ 30,000), both from the state of Yucatan, Mexico *Population 2:* Convenience sample of fracture records from Hospital O'Horan, a major government hospital in Merida, Yucatan, Mexico	*Population 1:* Any: 0 *Population 2:* Any: 1,085 (42.0%)	*Population 1:* Self-reported *Population 2:* Fracture records from hospital database	[a]	DO
New Zealand								
Adsett, 2013 [10]	Indigenous: 5,520 ([a]) Non-Indigenous: 21,117 ([a])	0+	1999–2009	Retrospective descriptive (temporal) study; cases identified from Ministry of Health (New Zealand) records	Facial: (26,637; 20.7%)	New Zealand Ministry of Health database: ICD-10 (Australian modification) fracture codes S02.0-S02.9, excluding S02.0 (fractures of base of skull) and S02.5 (fracture of tooth)	Road traffic accidents, falls, other/sport, self-harm, interpersonal violence, unspecified, war, medial, sequelae, supplemental, using ICD-10 'E' codes	DO
Buchanan, 2005 [11]	Indigenous: 812 ([a]) Non-Indigenous: 1,715 ([a])	0+	1989-2000	Retrospective descriptive (temporal) study; Cases with facial fracture attending the Maxillofacial and Oral Surgery Department, Waikato Hospital	Mandibular: (1,330; [a]) Zygomatic complex: (844; [a]) Dentoalveolar: (147;[a]) Le Fort (136; [a]) Orbital, including Blow-outs: (130: [a]) Others: (31; [a]) Combined: (2,618,32.1%)	[a]	Interpersonal violence, road traffic accident, falls, sport, other	DO
Kieser, 2002 [16]	Indigenous: [a] ([a]) Non-Indigenous: [a] ([a])	0+	1979–1998	Retrospective age-adjusted incidence rates per decade, using mean New Zealand population for the period as the standard; cases with facial fracture requiring inpatient treatment in public hospitals (first admission only)	Facial: (27,732; [a])	ICD-9 fracture codes 802.0 to 802.9, which includes nasal bones, mandible, malar and maxillary bones, orbit (excluding roof of orbit), alveolus and palate	Assault, motor vehicle accidents, struck (unintentional), struck (sport), fall (unintentional), fall (sport), other, all mechanisms; causes identified using ICD-9 'E' codes	IR
Norton, 1995 [32]	Indigenous: 16 (50%) Non-Indigenous: 1816 (77%)	≥60	1991–1994	Retrospective age-adjusted incidence rates, using the 1991 New Zealand male and female population aged 60 years or over as the standard; cases	Hip (femoral neck): (1,832; 0.9%)	ICD-9 code 820	[a]	IR

Table 2 (*continued*)

Author et al, year of publication	Study subjects (% women)	Age, presented as years, or mean (±SD)	Study period	Study design and population description	Skeletal fracture site (total fractures in sample; % sustained by Indigenous persons)	Fracture ascertainment, incl. ICD-9/10 codes where provided	Fracture cause, incl. ICD-9/10 codes where provided	Type of results: IR, MR, DO
				identified from records of admissions to the Middlemore and Auckland public hospitals from data held by the New Zealand Health Information Services				
Barber, 1995 [29]	Indigenous: 115 (70.4%) Non-Indigenous: 8,833 (78.4%)	≥60	1989–1991	Retrospective age-adjusted incidence rates per year, using mean New Zealand population for the period as the standard, whereby 1986 census was used for 1989 and 1990 population data, and 1990 census for 1991 population data; cases identified from patient admissions	Hip (femoral neck): (8,948; 1.3%)	ICD-9 code 820	[a]	IR
Koorey, 1992 [33]	Indigenous: [a] ([a]) Non-Indigenous: [a] ([a])	0+	1979–1988	Retrospective age-adjusted annualized incidence rates, using the overall New Zealand male and female population for the period as the standard; cases identified from admission records to all public hospitals, held by the National Health Statistical Services, New Zealand	Facial: (1,565; [a])	ICD-9 fracture codes 802.0 to 802.9, which includes nasal bones, mandible, malar and maxillary bones, orbit (excluding roof of orbit), alveolus and palate	Assault, Rugby Union and League, other sports, motor vehicle crashes, motor vehicle non-traffic, falls, cycle, animal riding, other, all causes; causes identified using ICD-9 'E' codes	IR
Stott, 1980 [26]	Indigenous: 148 (41.2%) Non-Indigenous: 4,498 (77.4%)	0+	1973–1977	Retrospective; incidence rates from cases for the Northland, Central and South Auckland statistical areas identified from records of admissions to all public hospitals held by the National Health Statistical Services, New Zealand	Hip (femoral neck): (4,646; 3.2%)	[a]	Falls, road traffic accidents, other	IR
United States of America								
Frech, 2012 [14]	Indigenous: [d] 8,039 (65.1%) Non-Indigenous: –	≥18	2004–2007	Retrospective cross-sectional prevalence study; recruited from EARTH study	Hip: ([a]; 100%) Vertebrae: ([a]; 100%) Wrist: ([a]; 100%) Any site: (1,669; 42.4% Alaska, 57.6% Navajo)	Self-reported fracture	[a]	DO
Nelson, 2011 [28]	Indigenous: 124 (100%) Non-Indigenous: [c] 10,324 (100%)	50-79	1994–2006	Retrospective cross-sectional study and incidence rates; subset population drawn from the prospective WHI-OS	Hip: ([a, a])	Self-reported hip fractures confirmed by local and central review of radiology reports (100% confirmed by blinded central adjudicators)	[a]	IR
Cauley, 2011 [12]	Indigenous: 88 (100%) Non-Indigenous: 2,144 (100%)	50–79	1994–2006	Prospective nested case-control, followed for mean 8 years; population drawn from the WHI	Any site, excluding fingers, toes, face, skull or sternum: (732; 6.3%)	Self-reported hip fractures confirmed by local and central review of radiology reports (100% confirmed by blinded central adjudicators);	[a]	DO

(*continued on next page*)

Table 2 (*continued*)

Author et al, year of publication	Study subjects (% women)	Age, presented as years, or mean (±SD)	Study period	Study design and population description	Skeletal fracture site (total fractures in sample; % sustained by Indigenous persons)	Fracture ascertainment, incl. ICD-9/10 codes where provided	Fracture cause, incl. ICD-9/10 codes where provided	Type of results: IR, MR, DO
						self-reported non-hip fractures confirmed by radiographic report and/or physician review of medical records (80% confirmed)		
Chen, 2010 [13]	Indigenous: 704 (100%) Non-Indigenous: 158,963 (100%)	50–79	1994–2006	Prospective cohort study followed for mean 7.8 years; incidence rates and multivariable modelling; population drawn from the WHI	Hip: (1,906; 0.4%) Vertebrae: (2,866; 0.3%) Any site, excluding fingers and toes: (26,694; 0.5%)	Self-reported hip fractures confirmed by local and central review of radiology reports (100% confirmed by blinded central adjudicators); self-reported non-hip fractures confirmed by radiographic report and/or physician review of medical records (70% confirmed)	[a]	DO
Cauley, 2007 [4]	Indigenous: 715 (100%) Non-Indigenous: 158,864 (100%)	50–79	1993–1998	Prospective annualized rates, study population drawn from the prospective WHI	Any site, excluding fingers, toes, face, skull or sternum: (23,270; 14.6%)	Self-reported hip fractures confirmed by local and central review of radiology reports (100% confirmed by blinded central adjudicators); self-reported non-hip fractures confirmed by radiographic report and/or physician review of medical records (80% confirmed)	[a]	IR, MR
Barrett-Connor, 2005 [30]	Indigenous: 1,708 (100%) Non-Indigenous: [c] 196,139 (100%)	≥50	1997–1998	Prospective cohort study with follow up of 1 year; incidence rates and multivariable modelling; community-dwelling postmenopausal women without known osteoporosis or a recent BMD test	Hip: (430; 0.5%) Wrist: (871; 1.0%) Wrist/arm: (1,087; 1.2%) Arm: (240; 0.2%) Vertebrae: (239; 0.1%) Rib: (698; 0.3%) Combined: (2,414; 1.8%)	Self-reported hip fractures validated by telephone with participant (~80% confirmed)	[a]	IR, MR
Pratt, 2001 [25]	Indigenous: 166 (74.1%) Non-Indigenous: –	≥64	1979–1989; 1996–1999	Retrospective; incidence rates using average of 1980 and 1990 census data as standard for 1985 population data, and 1997 estimates from Alaska Department of Labor as standard for 1997 population data; cases identified from the Alaska Native Medical Centre, Anchorage, Alaska. No non-indigenous reference population.	Hip: (166; 100%)	[a]	[a]	IR

Abbreviations: ADGs = Aggregated Diagnosis Groups; AFL = Australian Football League; BMD = bone mineral density; DO = descriptive only; EARTH = Education and Research Towards Health study; HMDS = Hospital Morbidity Data System; ICD = International Statistical Classification of Disease and Related Health Problems (9th or 10th revision); IR = incidence rates; FNIRHS = First Nations and Inuit Regional Health Survey; MR = multivariable results; SD = standard deviation; WHI = Women's Health Initiative.

[a] Data not provided.

[b] Indigenous status and sex for n = 4 fractures was unknown, however for analyses the authors had included the n = 4 as non-Indigenous persons.

[c] People included in the non-Indigenous population (% women), using authors' specific wording of categories: Nelson et al [28] = 8,156 non-Hispanic white (100%); 1,466 African-American (100%); 702 Mexican-American (100%) Barrett-Connor et al [30] = 179,470 Caucasian (90.7%); 7,784 black (3.9%); 1,912 Asian (1.0%); 6,793 Hispanic (3.5%) Cauley et al, 2011 [12] = 780 white (100%); 758 black (100%); 382 Hispanic (100%); 224 Asian (100%) Chen et al [13] = 4,140 Asian or Pacific Islander (100%); 14,417 African American (100%); 6,436 Hispanic or Latino (100%); 132,176 white, not of Hispanic origin (100%); 1,794 other (100%).

[d] People included in the Indigenous population (% women): Frech et al [14] = 2,709 Alaska Native (63.9%); 5,330 Navajo (65.7%).

3.3. Findings of the studies

3.3.1. Fracture rates

Table 3 presents incident fracture rates per 100,000 person-years for indigenous compared to non-indigenous populations, according to skeletal site of fracture and country, as reported in the individual studies. The results of re-standardized hip fracture rates for both sexes combined are presented in Fig. 1, whilst Supplementary Figs. 1 and 2 present the rates for women and men, respectively. Given that fracture rates from the Manitoban administrative health database were reflected in two papers (Leslie et al., 2004, 2006), albeit encompassing different time periods and participant numbers and demographics, only results from the larger analyses performed in 2004 are presented (Leslie et al., 2004). In addition, there was much methodological heterogeneity between studies that had presented multivariable modelling, age, sex, recruitment methods, site and cause of fracture, self-reported versus radiological identification of fracture, variables included within the modelling, and statistical analyses. Given this, we synthesised the results from all 5 studies that presented multivariable analyses (Canada = 3; USA = 2), rather than excluding a subset based on methodological

Table 3
Age-standardised incident fracture rates per 100,000 person years (95% CI) from studies that investigated fractures in indigenous compared to non-indigenous populations: results presented according to skeletal site, country, and alphabetically by surname of first author.

Country	Incidence rates per 100,000 person years (95% CI) *Indigenous*			*Non-indigenous*			Author et al, publication year
	Women	Men	Combined	Women	Men	Combined	
Hip							
Australia	300 ([d])	**130 ([d])**	–	300 ([d])	50 ([d])	–	MacIntosh, 2001 [22]
Australia	**302.8 (240.7–364.9)**	**244.6 (187.3–302.0)**	–	183.6 (179.7–187.4)	97.7 (94.2–101.3)	–	Wong, 2013 [27]
Non-metro	–	–	**303.2 (253.4–352.9)**	–	–	175.0 (168.1–81.9)	
Metropolitan	–	–	**222.7 (125.6–319.9)**	–	–	141.7 (138.8–144.7)	
Canada[g]	267 (133–479)	**247 (117–460)**	–	**411 (405–416)**	188 (184–191)	–	Jandoc, 2015 [15]
Canada	**96 (60–128)**	**70 (39–128)**	**84 (75–93)**	64 (46–90)	37 (23–59)	51 (47–55)	Leslie, 2004 [18]
New Zealand							Barber, 1995 [29]
1973–1975	239 (147–331)	149 (89–208)	192 (139–246)	**493 (476–510)**	**162 (151–173)**	**347 (337–358)**	
1989–1991	516 (355–566)	197 (117–243)	356 (263–388)	**827 (795–832)**	**288 (269–295)**	**589 (566–590)**	
New Zealand	151.6 ([d])	169.3 ([d])	–	**571.5 ([d])**	**314.6 ([d])**	–	Norton, 1995 [32]
New Zealand							Stott, 1980 [26][a]
65–69 years	79 ([d])	93 ([d])	–	**173 ([d])**	**650 ([d])**	–	
70–74 years	160 ([d])	–	–	**356 ([d])**	**138 ([d])**	–	
75–79 years	520 ([d])	**430 ([d])**	–	**670 ([d])**	273 ([d])	–	
80–84 years	780 ([d])	460 ([d])	–	**1,410 ([d])**	**540 ([d])**	–	
85 years +	680 ([d])	730 ([d])	–	**2,850 ([d])**	**1,360 ([d])**	–	
USA	[c]	–	–	[c]	–	–	Nelson, 2011 [28]
Humerus							
Canada[g]	252 (149–400)	135 (59–263)	–	**334 (330–339)**	**137 (134–140)**	–	Jandoc, 2015 [15]
Radius/ulna/wrist							
Canada[g]	**778 (576–1,027)**	192 (112–307)	–	682 (676–687)	**241 (237–244)**	–	Jandoc, 2015 [15]
Canada	**148 (100–218)**	**115 (72–183)**	**132 (120–143)**	50 (34–73)	41 (26–64)	45 (41–49)	Leslie, 2004 [18]
Spine, wrist, hip combined							
Canada	**416 (330–524)**	**338 (258–443)**	**378 (358–398)**	199 (164–241)	166 (133–208)	183 (175–191)	Leslie, 2004 [18]
Hip, humerus, radius/ulna combined							
Canada[g]	1,225 (958–1,544)	**538 (358–778)**	–	**1,289 (1,281–1,298)**	525 (520–531)	–	Jandoc, 2015 [15]
Craniofacial							
Canada	**440 (352–551)**	**930 (790–1,095)**	**674 (648–701)**	82 (60–110)	194 (158–238)	136 (129–143)	Leslie, 2004 [18]
Facial							
New Zealand	–	–	**68.1 ([d])**	–	–	34.2 ([d])	Kieser, 2002 [16]
New Zealand	**44.8 ([d])**	**152.0 ([d])**	–	15.4 ([d])	56.9 ([d])	–	Koorey, 1992 [33]
Jaw							
Australia	**174.6**[f]	**347.5**[f]	–	7.8[f]	44.8[f]	–	Kruger, 2006 [17]
Any type							
Canada	**2,965 (2,772–3,229)**	**3,404 (3,130–3,702)**	**3,175 (3,113–3,236)**	1,421 (1,322–1,526)	1,721 (1,606–1,843)	1,565 (1,540–1,589)	Leslie, 2004 [18]
USA	[c]	[c]	[c]	[c]	[c]	[c]	Barrett-Connor, 2005 [30]
USA	2,000[e]	–	–	2,000[b, e]	–	–	Cauley, 2007 [4]

Abbreviations: USA = United States of America.
For each study, bolded text indicates in which group the highest fracture rate was observed.
[a] Stott et al [26] presented incidence rates in 5 year age groups ranging from birth; only rates for age groups ≥65 years have been tabulated.
[b] Results tabulated for the non-indigenous populations include only 'White'/Caucasian populations.
[c] Standardised incidence rates were presented graphically, thus no rates were available for extraction.
[d] 95% confidence intervals (95% CI) not provided by study.
[e] Annualized (%) fracture rates, presented as per 100,000 person years.
[f] Only crude rates were available for extraction.
[g] Indigenous populations included only Metis.

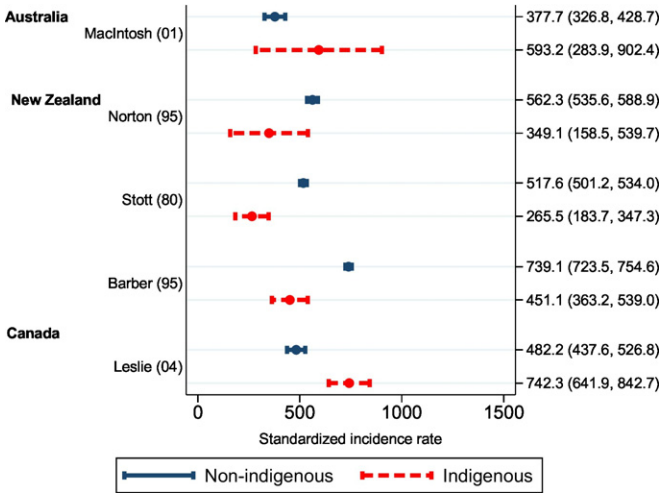

Fig. 1. Re-standardized hip fracture incidence rates for both sexes combined using the World Health Organization 2000–2025 reference population aged ≥65 years as standard. Bars represent 95% confidence intervals.

quality score, as had been proposed within our published protocol (Brennan-Olsen et al., 2016).

3.3.1.1. Hip fracture. After re-standardizing to the WHO reference population, and with both sexes combined, indigenous persons from New Zealand (Stott et al., 1980; Barber et al., 1995) showed consistently lower rates of hip fracture compared to their continent-specific non-indigenous counterparts; however, the opposite was observed in a study from Canada (Leslie et al., 2004) and a study from Australia (MacIntosh and Pearson, 2001) (Fig. 1). Larger variability between continents was observed in female populations, especially among indigenous groups. Continent-specific differences were observed when results were confined to women only (Supplementary Fig. 1), with three studies from New Zealand (Stott et al., 1980; Barber et al., 1995; Norton et al., 1995) showing statistically lower rates of hip fracture for indigenous compared to non-indigenous women; however, higher rates for indigenous compared to non-indigenous women were reported for Australia (Wong et al., 2013), Canada (Leslie et al., 2004) and the USA (Pratt and Holloway, 2001). Results were similar for men (Supplementary Fig. 2), where statistically different variations in hip fracture rates were observed in one study from New Zealand (Barber et al., 1995) that reported lower rates for indigenous men compared to their non-indigenous counterparts, whilst higher rates for indigenous men were observed in Australia (Wong et al., 2013) and Canada (Leslie et al., 2004).

3.3.1.2. Wrist, humerus and radius/ulna fracture. For humerus fractures, 252 fractures per 100,000 person-years were reported by Metis women from Canada compared to 334 in their non-indigenous counterparts, whilst Metis and non-indigenous men had similar fracture rates of 135 and 137 per 100,000 person years, respectively (Jandoc et al., 2015). Incidence rates for fracture of the radius/ulna in Canada were 778 per 100,000 person-years in Metis women compared to 682 for non-indigenous women; for men the rates were 192 in Metis men compared to 241 in non-indigenous men (Jandoc et al., 2015). For all First Nations persons combined, fracture rates for indigenous women were almost three-fold greater than non-indigenous women (148, 95%CI 100–218, vs. 50, 95%CI 34–73, respectively) (Leslie et al., 2004). Similar observations were observed for First Nations compared to non-indigenous men with a two-fold greater rate of fractures (115, 95%CI 72–183, vs. 41, 95%CI 26–64, respectively) (Leslie et al., 2004).

3.3.1.3. Hip, humerus and radius/ulna fracture combined. Incident rates of fractures of the hip, humerus and radius/ulna combined, also reported in only one of the identified studies, were 1225 for Metis women from Canada compared to 1289 per 100,000 person-years for non-indigenous women, whilst for men the corresponding values for Metis compared with non-indigenous were similar, being 538 and 525, respectively (Jandoc et al., 2015).

3.3.1.4. Craniofacial, facial and jaw fracture. Craniofacial fractures per 100,000 person-years in Canada were more than four times greater for First Nations women compared to their non-indigenous counterparts (440, 95%CI 352–551, vs. 82, 95%CI 60–110, respectively); rates for men were higher than for women, and were almost five times greater for First Nations men compared to non-indigenous men (930, 95%CI 790–1095, vs. 194, 95%CI 158–238, respectively) (Leslie et al., 2004). Facial fractures per 100,000 person-years in New Zealand were 44.8 in indigenous women compared to 15.4 in their non-indigenous counterparts, and were 152.0 and 56.9 for indigenous compared to non-indigenous men, respectively (Koorey et al., 1992). In Australia, fractures of the jaw per 100,000 person-years were 22 times greater in indigenous compared to non-indigenous women (174.6 vs. 7.8, respectively); in men the incidence rates were nearly 8 times greater for indigenous compared to non-indigenous men (347.5 vs. 44.8, respectively) (Kruger et al., 2006).

3.4. Multivariable results

Table 4 presents results from the five studies that performed multivariable analyses to investigate the risk of fracture in indigenous compared to non-indigenous populations. The two USA studies each reported that no association was observed between fracture and indigenous status (Cauley et al., 2007; Barrett-Connor et al., 2005). In comparison, a two- to three-fold increased risk of osteoporotic fracture and a four- to five-fold increased risk of craniofacial fracture for indigenous compared to non-indigenous populations was reported within the three Canadian studies that had investigated the Manitoba population, albeit from different time periods (Leslie et al., 2004, 2005, 2006).

3.5. Risk factors for differences in fracture

The prevalence of diabetes was independently associated with an increased likelihood of osteoporotic fracture (RR 1.13, 95%CI 1.02–1.25), and of hip fracture (RR 1.48, 95%CI 1.12–1.97) for Canadian indigenous persons compared to their non-indigenous counterparts (Leslie et al., 2006), with longer duration of diabetes increasing the risk. That study also reported comorbidity and substance abuse, as a proxy for high alcohol consumption, contributed to greater fracture risk in indigenous compared to non-indigenous populations (Leslie et al., 2006). Lower income was another significant predictor of wrist, spine or craniofacial fracture (RR 1.51, 95%CI 1.03–2.21; RR 1.59, 95%CI 1.23–2.06; RR 1.66, 95%CI 1.41–1.95, respectively) (Leslie et al., 2005). Fracture history was identified as increasing the risk of fracture three-fold for indigenous populations from the USA compared to their non-indigenous counterparts (HR 2.9, 95%CI 1.5–5.7), whilst current hormone treatment was reported to be protective (HR 0.5, 95%CI 0.3–0.9) (Cauley et al., 2007). In the studies that had adjusted for vitamin D status, no increased risk was reported.

4. Discussion

We report that, after standardization to the WHO reference population, incidence rates of hip fracture were lower for indigenous persons from all countries, with the exception of Canada and Australia where greater rates of hip fractures were observed in indigenous persons compared to their non-indigenous counterparts. However, for craniofacial, facial and/or jaw fractures, the incidence rates were up to 22 times greater for indigenous compared to non-indigenous women, and eight times greater for indigenous compared to non-indigenous men. In

Table 4
Key results of included articles that performed multivariable analyses, including modelling procedures, key results and summary of associations: studies presented under country of origin, and then chronologically according to year of publication.

Author et al, publication year	Multivariable modelling procedures	Key results of fracture risk for indigenous populations (non-indigenous held as referent)	Summary of associations for indigenous populations compared to non-indigenous populations
Canada			
Leslie, 2006 [21]	Poisson regression models adjusted for age (10 year age groups), sex, area of residence, income quintile, substance abuse (proxy for alcohol consumption), diabetes, number of ADGs	Osteoporotic fracture: RR 1.99 (95% CI 1.84–2.16) Hip fracture: RR 2.05 (95% CI 1.53-2.75)	~two-fold increased risk of osteoporotic or hip fracture
Leslie, 2005 [3]	Poisson regression models (cases and controls matched by year of birth, sex and geographic area of residence) adjusted for age (10 year age groups), sex, income, diabetes, interaction terms (age * sex, income * geographic area of residence)	Any fracture: RR 2.06 (95% CI 2.00–2.12) Hip fracture: RR 2.03 (95% CI 1.72–2.38) Wrist fracture: RR 2.31 (95% CI 2.01–2.65) Vertebral fracture: RR 1.70 (95% CI 1.52–1.90) Craniofacial fracture: RR 3.90 (95% CI 3.64–4.19)	~two-fold increased risk of any, hip, wrist, or spine fracture and ~four-fold increased risk of craniofacial fracture
Leslie, 2004 [18]	Standardized incidence ratios (SIRs) calculated (indigenous and non-indigenous cohorts matched for sex and age); models for both sexes combined adjusted for sex and age (5 year age groups), and sex-specific models adjusted for age (5 year age groups)	*Both sexes combined* Any fracture: SIR 2.23 (95% CI 2.18–2.29) Hip fracture: SIR 1.88 (95% CI 1.61–2.14) Wrist fracture: SIR 3.01 (95% CI 2.63–3.42) Spine fracture: SIR 1.93 (95% CI 1.79–2.20) Craniofacial fracture: SIR 5.07 (95% CI 2.18–2.29) *Men only* Any fracture: SIR 2.19 (95% CI 2.12–2.27) Hip fracture: SIR 2.13 (95% CI 1.68–2.63) Wrist fracture: SIR 2.83 (95% CI 2.29–3.39) Spine fracture: SIR 1.75 (95% CI 1.54–2.08) Craniofacial fracture: SIR 4.89 (95% CI 4.51–5.29) *Women only* Any fracture: SIR 2.26 (95% CI 2.20–2.36) Hip fracture: SIR 1.75 (95% CI 1.41–2.05) Wrist fracture: SIR 3.16 (95% CI 2.68–3.79) Spine fracture: SIR 2.12 (95% CI 1.88–2.51) Craniofacial fracture: SIR 5.48 (95% CI 4.88–6.19)	*Both sexes combined* ~two-fold increased risk of any, hip, or spine fracture; three-fold increased risk of wrist fracture; and five-fold increased risk of craniofacial fracture *Men only* ~two-fold increased risk of any, hip, or spine fracture; three-fold increased risk of wrist fracture; and five-fold increased risk of craniofacial fracture *Women only* ~two-fold increased risk of any, hip, or spine fracture; three-fold increased risk of wrist fracture; and > five-fold increased risk of craniofacial fracture
United States of America			
Cauley, 2007 [4]	Multivariate model adjusted for age, years since menopause, education, living with partner, parental fracture, weight, height, caffeine intake, current smoking, history of fracture, current hormone therapy, corticosteroid use, sedatives/antiolytics, history of arthritis, depression, health status, parity	Any fracture: HR 0.95 (95% CI 0.75–1.20)	Not significant
Barrett-Connor, 2005 [30]	Cox proportional hazards model, adjusted for age, education, current health status, years since menopause, weight, estrogen use, cortisone use, smoking, regular exercise, alcohol use, BMD site/device	Osteoporotic fracture: RR 0.87 (95% CI 0.57–1.32) Non-wrist fracture: RR 0.59 (95% CI 0.32–1.10)	Not significant

Results presented as adjusted Odds Ratio (OR), Relative Risk (RR), Hazard Ratios (HR) or β = beta coefficient, and 95% confidence intervals (95% CI).
Abbreviations: ADGs = Aggregated Diagnosis Groups; BMD = bone mineral density; BMI = body mass index.

multivariable analyses that adjusted for socio-demographic and clinical risk factors, indigenous persons were two to three times more likely to experience an osteoporotic fracture and four to five times more likely to experience a trauma-related fracture compared to non-indigenous persons. Risk factors associated with an increased likelihood of fracture were diabetes, substance abuse, comorbidity, lower income, geographic locality, and fracture history, whilst current hormone treatment had a protective effect.

4.1. Differences in fracture rates and risk

The observed differences in hip fracture rates in indigenous compared to non-indigenous populations appear to be continent-specific. For women, First Nations peoples from Canada, Alaskan Inuit peoples from the USA and indigenous persons from Australia appeared to have greater fracture rates than their non-indigenous counterparts. For men, First Nations peoples form Canada, and indigenous persons from Australia had greater hip fracture rates than their non-indigenous counterparts. Our findings suggest that Maori peoples from New Zealand had lower fracture rates than their non-indigenous counterparts, and this was consistent for both sexes. However, comparability between studies should be acknowledged with regards to method of fracture ascertainment. For instance in those studies that investigated indigenous status and hip fractures by self-report, no associations between fractures and indigenous status were observed. In contrast, in the studies that ascertained hip fractures using ICD codes or radiographic evidence, the risk of fracture was approximately twice as likely for indigenous persons compared to non-indigenous persons. Apart from methodological concerns that demand care be taken when interpreting results from individual studies, there are likely to be many varied reasons for differences in fracture rates and risk according to indigenous status. Elucidation of reasons for these differences may be informed by reference to a biomedical versus eco-social dichotomy (Leslie and Lentle, 2006); notably, similar dichotomized constructs have been suggested by others (Megyesi et al., 2011). However, due to complex and inextricable links between biomedical and eco-social factors, a combination of both is more likely, rather than any independent influence; nonetheless, these constructs provide a foundation on which to base speculations.

4.1.1. Biomedical factors

Continent-specific differences in fracture rates, similar to that observed in Canadian compared to New Zealand indigenous populations, may be explained by an effect of latitude on fracture risk (Johnell et al., 2007), although based on a paucity of data we are unable to speculate further. However, a factor of which more is known, is the effect of a larger body or bone size on fracture (Johansson et al., 2014); which may offer a potential explanation regarding the different fracture rates for indigenous compared to non-indigenous persons, as was observed in those studies that employed clinically-ascertained fractures. For instance, higher levels of age-, height-, and percentage body fat-adjusted BMD among Maori men and women compared to their European counterparts have been reported (Swinburn et al., 1999), and similar findings have also been shown in Canadian First Nations peoples compared to their non-indigenous counterparts (Leslie et al., 2008); indeed, an earlier Greenland-based study showed that body size appeared to explain any differences in BMD between Inuit and Caucasian populations (Andersen et al., 2005). Leslie and Lentle (2006) suggested that correcting for bone size by way of bone mineral apparent density (BMAD), rather than BMD per se, may avoid an underestimation of fracture risk. Another factor influencing fracture rates may be the difference in life expectancies between indigenous and non-indigenous populations, given that hip fractures are highly prevalent after the seventh decade of life we speculate that a reduced life expectancy may explain some of the lower rates of hip fracture observed in non-indigenous persons compared to their non-indigenous counterparts. As we have previously identified (Brennan-Olsen et al., 2016), indigenous persons from Australia have an average life expectancy of 59.5 years that is indicative of a ~10 year gap in longevity (Cooke et al., 2007; Rosenstock et al., 2013), First Nations peoples from the USA live an average of 70.8 years (Cooke et al., 2007), Maoris from New Zealand live an average of 71.1 years (Cooke et al., 2007), and First Nations, Metis and Inuit peoples from Canada live an average of 72.8 years (Cooke et al., 2007).

Despite much heterogeneity between studies, some risk factors were identified as being associated with fracture risk for indigenous compared to non-indigenous persons. In one of the USA-based studies, fracture history increased the likelihood of fracture for indigenous persons whilst current hormone therapy offered some protection (Cauley et al., 2007). Having a greater number of comorbid conditions was associated with increased fracture risk for indigenous persons, as was diabetes alone (Leslie et al., 2006). Indeed, indigenous populations have a disproportionately greater prevalence of chronic diseases, especially diabetes (Young et al., 2000; McDermott et al., 2010; Joshy and Simmons, 2006), and altered bone metabolic markers (Schwartz, 2003) and a higher fracture risk have both been reported in populations with diabetes (Oei et al., 2015). Independent of indigenous status, however, there are numerous risk factors associated with an increased risk of fracture: notable are the clinical risk factors included within the WHO's 10 year fracture risk calculator (FRAX) (Kanis et al., 2009). We acknowledge that these factors may indirectly or directly influence fracture risk, independent of indigenous status.

4.1.2. Eco-social factors

The clinical risk factors included in FRAX could equally fall within, and be inextricably linked with, the eco-social construct. Lifestyle and risk-taking behaviours known to be associated with increased fracture risk are, in the majority, highly socially patterned (Brennan et al., 2014); these include smoking (Hiscock et al., 2012) and alcohol consumption (Mulia et al., 2008). However, even the prevalence of chronic diseases associated with fracture risk vary according to socioeconomic status, for instance diabetes (Krishnan et al., 2010; Agardh et al., 2007) and fracture history (Brennan et al., 2015). Our review showed substance abuse to be associated with a higher risk of fracture in indigenous populations (Leslie et al., 2006), as were lower income and area of geographic residence (Leslie et al., 2005).

Not only do indigenous populations worldwide have a heavy burden of social, environmental and medical issues (MacMillan et al., 1996), but intentional or non-intentional trauma-related injuries from motor vehicle accidents or interpersonal violence are disproportionately experienced by indigenous persons from Canada, Australia and New Zealand compared to their non-indigenous counterparts (Karmali et al., 2005; Kieser et al., 2002; Jayaraj et al., 2012). A study by Karmali et al. (2005) reported on the risk of injury associated with specific causes in the Canadian population and reported that, compared to non-indigenous persons, indigenous persons had a three-fold greater risk of injuries related to road traffic accidents, and eleven times the risk of injuries caused by interpersonal violence. Given this, the cause of fracture is imperative to consider when investigating differences in fracture rates between indigenous and non-indigenous populations; indeed, cause of injury may be correlated with skeletal site of fracture. Our review found that for craniofacial fractures, indigenous men and women from Canada, New Zealand, and Australia had greater rates than their non-indigenous sex-specific counterparts; of the sexes, women had a greater rate of fractures at these sites than men. The underlying causes for trauma-related fractures are beyond the scope of this review, yet likely a symptom of complex psychosocial, economic and cultural issues for which urgent action is necessary.

4.2. Strengths and weaknesses

Our review has a number of strengths. Firstly, the study selection and data extraction were confirmed by two authors, and the assessment of methodological quality was independently performed by two authors initially blinded to the results of the other. The definition of indigenous status employed within this review aligned with Article 33 of the *United Nations Declaration on the Rights of Indigenous Peoples* (United Nations, 2007), whereby the importance of self-identification as an indigenous person is emphasized. This is the first review of its kind to report fracture incidence rates and risk factors for fracture between indigenous and non-indigenous populations. In addition, we performed ad-hoc analyses by re-standardizing incident hip fracture rates using the

WHO reference population as standard, in order to account for much heterogeneity between studies and to provide a more just comparison of fracture incidence rates between countries.

Our review also has a number of limitations. As mentioned, the reviewed studies were heterogeneous which precluded undertaking meta-analyses; however, given the argument that continentally-defined indigenous groups should be investigated separately, our re-standardization analyses enabled a more equitable comparison. We identified studies from only four different countries, with some skeletal sites (humerus, radius/ulna and jaw) investigated by only one study each. In addition, five of the Canadian studies had investigated populations in the Province of Manitoba; however, these analyses are each distinct with regards to time periods, population numbers and demographics, and analytical approach. Clearly, the vast cultural diversity in indigenous populations is not paralleled with the diversity of available literature. The lack of associations observed in studies from the USA may be influenced by small sample sizes of indigenous persons; an issue acknowledged by Barrett-Connor et al. (2005), a study that actually had the largest sample of indigenous persons of all the USA-based studies. The findings of our review could be influenced by a type II error inherent within the reviewed studies, which was reported with regards to hospitalization data ascertained from the New Zealand Health Information Service from which a 7.4% underestimation of the true incidence of hip fracture was reported by Norton et al. (1995); however, that underestimation issue was reported more than two decades ago, is therefore only likely to influence publications from that era. Finally, cause of fracture may likely bias some results; for instance, the only study from Canada to report higher rates of hip fracture in indigenous compared to non-indigenous men was that by Jandoc et al. (2015), of which Metis were the only indigenous persons included in the study, rather than the First Nations population as per the work by Leslie et al. (2006). Similarly, the method of fracture ascertainment may explain some observed differences in fracture rates.

5. Conclusion

In conclusion, we suggest there to be many varied reasons for differences in fracture rates and risk according to indigenous status. We observed a worldwide paucity of data that indicates an urgent need for further research regarding indigenous status and fracture epidemiology and aetiology. However, taking into account this paucity of data, we reported that, compared to non-indigenous populations: (1) indigenous persons from Canada and Australia had higher rates of hip fractures, however, the opposite was observed for indigenous persons from all other countries; (2) significantly greater rates of trauma-related fractures were observed in indigenous persons, specifically craniofacial fractures; and (3) factors associated with an increased risk of fracture for indigenous persons including diabetes, substance abuse, medical comorbidity, lower income, locality and fracture history. Our findings have implications for healthcare professionals and communities to enhance the prevention of trauma-related fractures in indigenous persons, and to focus on the modifiable lifestyle behaviours to help reduce osteoporotic fractures in all populations. Our findings also indicate the imperative to account for indigenous status in future studies investigating fracture outcomes, and analyses should ideally focus on site-specific and cause-specific fracture.

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Conflict of interest

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