

Validity of Major Osteoporotic Fracture Diagnoses in the Danish National Patient Registry

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Objective: To evaluate the validity of diagnosis codes for Major Osteoporotic Fracture (MOF) in the Danish National Patient Registry (NPR) and secondly to evaluate whether the fracture was incident/acute using register-based definitions including date criteria and procedural codes.

Methods: We identified a random sample of 2400 records with a diagnosis code for a MOF in the NPR with dates in the year of 2018. Diagnoses were coded with the 10th revision of the International Classification of Diseases (ICD-10). The sample included 2375 unique fracture patients from the Region of Southern Denmark. Medical records were retrieved for the study population and reviewed by an algorithmic search function and medical doctors to verify the MOF diagnoses. Register-based definitions of incident/acute MOF was evaluated in NPR data by applying date criteria and procedural codes.

Results: The PPV for MOF diagnoses overall was 0.99 (95% CI: 0.98;0.99) and PPV=0.99 for the four individual fracture sites, respectively. Further, analyses of incident/acute fractures applying date criteria, procedural codes and using patients' first contact in the NPR resulted in PPV=0.88 (95% CI: 0.84;0.91) for hip fractures, PPV=0.78 (95% CI: 0.74;0.83) for humerus fractures, PPV=0.78 (95% CI: 0.73;0.83) for clinical vertebral fractures and PPV=0.87 (95% CI: 0.83;0.90) for wrist fractures.

Conclusion: ICD-10 coded MOF diagnoses are valid in the NPR. Furthermore, a set of register-based criteria can be applied to qualify if the MOF fracture was incident/acute. Thus, the NPR is a valuable and reliable data source for epidemiological research on osteoporotic fractures.

Keywords: major osteoporotic fractures, validity, positive predictive value, the Danish National Patient Register, algorithmic search function, epidemiology

Introduction

Osteoporosis is a systemic skeletal disease characterized by low bone mass and deterioration of bone tissue, leading to increased bone fragility and susceptibility to fracture.¹ The disease osteoporosis is often undetected until an osteoporotic fracture occurs. While osteoporosis leads to an increased risk of low-trauma and non-traumatic fractures at classical osteoporotic anatomical sites, often referred to as minor osteoporotic fractures or fragility fractures, epidemiological studies have also demonstrated that patients with osteoporosis are at increased risk of high energy fractures.² A Major Osteoporotic Fracture (MOF) is a commonly applied fracture outcome definition in research settings, and includes hip, clinical vertebral, wrist or humerus fractures.^{3–8} MOF will be the main focus of this study. For studies performed in administrative data, such as in registers or databases, MOF can be defined through diagnoses coded using the International Classification of Diseases (ICD).⁹ However, diagnostic coding of MOFs in register data is liable to several limitations that may lead to misclassification. Firstly, the validity of diagnosis codes for MOFs is unknown in the vast majority of registers or databases.¹⁰ Secondly, it is not always possible to ascertain if the fracture is incident/acute or not, as the diagnoses code could be given in relation to a later

clinical examination in the outpatient clinic. Thus, this study aimed to evaluate the validity of diagnosis codes for Major Osteoporotic Fracture (MOF) in the Danish National Patient Registry (NPR) and secondarily evaluate whether the fracture was incident/acute using register-based definitions including date criteria and procedural codes. The latter could provide further corroboration through identification of relevant radiology studies and surgery consistent with incident/acute fracture diagnosis and care. The findings from this study may be relevant for future studies where MOF are solely identified through registers. This is both relevant with respect to epidemiological studies on osteoporosis, but could also be of importance if administrative health data are to be used in screening or personalized medicine approaches.

Materials and Methods

This study reviewed medical records of a random sample of 2400 ICD-10 coded MOF contacts identified in the NPR from the year of 2018. The total study population included 2375 individuals (some individuals were represented with multiple contacts). Bone mass declines with age, therefore, patients aged 45 years and above on January 1 2018 were selected to reduce the risk of including younger patients diagnosed with MOF due to other underlying conditions. Fracture contacts were randomly sampled from the following hospitals in the Region of Southern Denmark: Odense University Hospital, Southern Jutland Hospital, Southwest Jutland Hospital, Kolding Hospital and Vejle Hospital. We sampled 2400 MOF contacts on the basis of a power calculation which resulted in n=2400 medical records to test a positive predictive value of 90% with an adequate statistical power of 80%. The sample was subcategorized into four fracture sites: hip fracture (n=600), clinical vertebral fracture (n=600), wrist fracture (n=600) and humerus fracture (n=600). ICD-10 coding for diagnoses, imaging studies and surgical procedures is provided in Table 1.

The Danish National Patient Registry (NPR)

The NPR is a national hospital register containing records on all contacts from Danish hospitals.¹¹ Diagnostic coding according to the ICD are available for each contact.¹¹ The NPR was used to identify a random sample of 2400 hospital contacts from public hospitals in the Region of Southern Denmark with MOF diagnoses during the year of 2018. Both primary and secondary diagnosis codes qualified for inclusion in this study. The data was extracted by the Danish Health Data Authority with the purpose of retrieving the corresponding patient medical records for review. ICD-10 codes in the data extraction were in use at Danish hospitals in the year 2018.

Table 1 NPR Coding of MOF Diagnoses, Imaging Studies and Surgical Procedures for MOF Fracture Sites

Fracture Site	Diagnoses (ICD-10)	Imaging Studies	Surgical Procedures
Hip fracture	S720*, S721*, S722*	UXRG10*, UXRG15*, UXMG10*, UXMG15*, UXCG10*, UXCG15*	KNFB*, KNFJ4*-9*
Humerus fracture Fracture of humerus (proximal)	S422*, S423*	UXRF15*, UXRF20*, UXCF15*, UXCF20*	
Clinical vertebral fracture Fracture of lumbar spine (lumbar VF) Fracture of spine, unspecified level Fracture of thoracic spine (thoracic VF) Fracture of cervical vertebrae	S320* DT08* S220*, S221* S120*, S121*, S122*	UXRE30*, UXCE30* UXRE20*, UXCE20* UXRE10*, UXCE10*	
Wrist fracture Fracture of forearm (distal)	S525*, S526*	UXRF30*, UXRF40*, UXRF45*, UXMF45*	

Note: *Substring characters were included eg DS721A, DS721B etc.

Abbreviations: NPR, National Patient Registry; MOF, Major Osteoporotic Fracture.

Medical Records (Cosmic Data)

Medical records were obtained from Cosmic, which contain all hospital records from the region of Southern Denmark from 2013 to 2022. Cosmic is an electronic software system and all medical records are fully digitalized. Medical records were retrieved for the 2375 fracture patients for the period of June 30 2017 to December 31 2018. This allowed a lookback period of a minimum of 6 months prior to the fracture date extracted from the NPR to assess when the fracture occurred (ie, if the identified medical record in 2018 was actually a follow-up for prior fracture). Cosmic data included all text material that was identifiable in the records from the study period (primarily record notes and radiological interpretations). The medical records were considered as the gold standard.

Algorithmic Search Function

To validate the 2400 MOF contacts from the NPR in the medical record text from Cosmic, a search function was developed with key words indicative of bone fracture. Keywords were selected by medical doctors. Thereafter we used word embeddings¹² trained on 300,000 medical records to retrieve a list of other fracture indicating words specific to the study population in the current study. The list was then manually reviewed before being applied to identify fractures in the medical records (list provided in [Table S1](#)). This approach was used successfully in another study using similar data.¹³ The algorithmic search function identified all fracture indicating text passages in the record text material. Identified text passages were then reviewed by medical doctors to assess if and when the fracture first occurred.

Medical Record Review

Medical doctors reviewed text passages identified by the algorithmic search function and classified fracture contacts as verified/unverified/unable to verify. In cases of doubt an orthopedic surgeon was consulted. Furthermore, the exact date of when the fracture first occurred was recorded.

Qualification of Incident/Acute MOF in the NPR with Date Criteria, Procedural Codes and Grace Periods

To investigate the potential for further qualification of the definition of MOFs in the NPR, a set of assumptions were tested for those MOF contacts where the NPR date corresponded to the fracture date assessed through medical record review. Incident/acute status were assumed if patients were registered in the NPR with an imaging study (x-rays, CTs or MRIs) and/or a surgical procedure (only hip fractures) on the same date or within 7 days after the NPR date. Two radiographers assessed and contributed with eligible administrative codes for imaging studies for each fracture site and surgical procedures were chosen as suggested by Hjelholt et al.¹⁴ It was furthermore assumed that incident/acute status would differ between contacts depending on whether the contact was the fracture patient's first or later in the register with the diagnosis. Lastly, it was assumed that a grace period of 30, 60, 90 or 180 days could be introduced between fracture dates to avoid classifying an earlier fracture as new.

Statistical Analyses

Statistical analyses included study population characteristics of fracture patients and calculations of positive predictive value (PPV). For MOFs overall and for each fracture site, PPVs with exact binomial 95% confidence intervals (CI) were calculated as the proportion of fracture diagnoses in the random NPR sample confirmed through medical record review. To examine incident/acute definitions of MOF, date criteria and procedural codes were applied to the PPV analysis to answer the secondary aim of the study. PPV was calculated for verified diagnoses of which patients had NPR registrations of imaging studies (all four fracture sites) and surgical procedures (only hip fractures) within +7 days of the confirmed fracture date. This was calculated as the proportion of the random data extraction that had registrations of imaging studies and surgical procedures in the NPR within +7 days of the NPR date. For this analysis only diagnoses that were verified in medical records on the same date as the randomly extracted NPR fracture date were included to ensure that the analysis included incident/acute fractures. The analysis was repeated on the part of the NPR data extraction where the contact was the patients' 1st registration in the register with the fracture diagnosis in years 2017–18 (2 years) and also on the remaining part of the NPR data extraction where the contact was the patients' 2nd or later (≥ 2 nd) on same

fracture site. Further, PPV was calculated for verified diagnoses as the proportion of the fracture diagnoses from the random data extraction where the contact was the ≥ 2 nd in the NPR with grace periods of ≥ 30 , ≥ 60 , ≥ 90 and ≥ 180 days, respectively, between the 1st and the ≥ 2 nd fracture date (coding provided in Table 1).

Sensitivity Analyses

Two sensitivity analyses were performed to investigate the effect on results when applying delay periods between registration dates. Firstly, PPV was calculated for verified diagnoses of which patients had NPR registrations of imaging studies (all four fracture sites) and surgical procedures (only hip fractures) within $-/+7$ days of the confirmed fracture date. Secondly, an analysis was performed on the part of the random NPR data extraction that were verified in medical records on the same date or on the date before (-1 day). In this analysis PPV was calculated for verified diagnoses of which patients had NPR registrations of imaging studies and surgical procedures (only hip fractures) within $+7$ days of the confirmed fracture date.

All analyses were performed in Stata version 17 or 18.^{15,16}

Results

Main Analysis

The majority of the study sample were women (71%), and the median (Q1;Q3) age was 73 (64;83) years (Table 2).

PPV of MOF Diagnoses in the NPR

The total sample constituted 2400 fracture contacts randomly extracted from the NPR of which 2375 contacts were verified in medical records, resulting in PPV=0.99 (95% CI: 0.98;0.99). Fracture site specific PPVs were PPV=0.99 (95% CI: 0.98;1.00) for hip fractures, PPV=0.99 (95% CI: 0.98;1.00) for humerus fractures, PPV= 0.99 (95% CI: 0.97;0.99) for clinical vertebral fractures and PPV= 0.99 (95% CI: 0.98;1.00) for wrist fractures (Table 2).

Application of Date Criteria, Procedural Codes and Grace Periods to Define Incident/Acute Fractures

Of the total 2400 MOFs, 1332 were verified in medical records on the same fracture date obtained from the NPR resulting in PPV=0.55 (95% CI: 0.53;0.58) (Table 3). Fracture site specific PPVs were PPV=0.69 (95% CI: 0.65;0.73) for hip fractures, PPV=0.47 (95% CI: 0.43;0.52) for humerus fractures, PPV=0.47 (95% CI: 0.43;0.51) for clinical vertebral fractures and PPV=0.58 (95% CI: 0.54;0.62) for wrist fractures. For all four fracture sites PPVs improved by including a criteria of a NPR registration of a relevant imaging study within $+7$ days of the fracture date. In hip fractures the PPV

Table 2 Study Population Characteristics and PPVs in Random NPR Data Extraction of ICD-10 Coded MOFs Verified Through Medical Record Review

Diagnoses	Total, N (%)	Female, N (%)	Age on Date of Fracture, Median (Q1;Q3)	Verified ICD-10 Through Medical Record Review, N/ Total, N
MOF PPV (95% CI)	2400	1697 (71)	73 (64;83)	2375/2400 0.99 (0.98;0.99)
Hip Fracture PPV (95% CI)	600	405 (68)	82 (73;89)	596/600 0.99 (0.98;1.00)
Humerus fracture PPV (95% CI)	600	457 (76)	72 (63;79)	594/600 0.99 (0.98;1.00)
Clinical vertebral fracture PPV (95% CI)	600	349 (58)	73 (62;81)	592/600 0.99 (0.97;0.99)
Wrist fracture PPV (95% CI)	600	486 (81)	70 (61;78)	593/600 0.99 (0.98;1.00)

Abbreviations: PPV, Positive Predictive Value; MOFs, Major Osteoporotic Fractures.

Table 3 PPVs of ICD-10 Coded MOF Diagnoses Verified in Medical Records on Same Date with Imaging Studies and Surgical Procedures Within + 7 Days in the NPR by All Diagnoses, by Diagnoses Where the Admission Date* is the 1st in the NPR and by Diagnoses Where the Admission Date is the ≥2nd in the NPR

Diagnoses	Total ICD-10	Verified on Same Date, N/N Total	Imaging Studies in the NPR (+7 Days), N/N Total	Surgical Codes in the NPR (+7 Days), N/N Total	Surgical Codes and Imaging Studies in the NPR (+ 7 Days), N/N Total
All PPV (95% CI)	N=2400	N=1332/2400 0.55 (0.53;0.58)			
Hip Fracture PPV (95% CI)	600	416/600 0.69 (0.65;0.73)	413/517 0.80 (0.76;0.83)	386/505 0.76 (0.72;0.80)	385/463 0.83 (0.79;0.86)
Humerus fracture PPV (95% CI)	600	285/600 0.47 (0.43;0.52)	279/515 0.54 (0.50;0.59)	NA NA	NA NA
Clinical vertebral fracture PPV (95% CI)	600	284/600 0.47 (0.43;0.51)	196/295 0.66 (0.61;0.72)	NA NA	NA NA
Wrist fracture PPV (95% CI)	600	347/600 0.58 (0.54;0.62)	340/474 0.72 (0.67;0.76)	NA NA	NA NA
1st NPR admission date PPV (95% CI)	N=1733	N=1266/1733 0.73 (0.71;0.75)			
Hip Fracture PPV (95% CI)	474	392/474 0.83 (0.79;0.86)	390/446 0.87 (0.84;0.90)	365/434 0.84 (0.80;0.87)	365/415 0.88 (0.84;0.91)
Humerus fracture PPV (95% CI)	376	276/376 0.73 (0.69;0.78)	271/346 0.78 (0.74;0.83)	NA NA	NA NA
Clinical vertebral fracture PPV (95% CI)	460	264/460 0.57 (0.53;0.62)	189/241 0.78 (0.73;0.83)	NA NA	NA NA
Wrist fracture PPV (95% CI)	423	334/423 0.79 (0.75;0.83)	328/377 0.87 (0.83;0.90)	NA NA	NA NA
≥2nd NPR admission date PPV (95% CI)	N=667	N=66/667 0.10 (0.08;0.12)			
Hip Fracture PPV (95% CI)	126	24/126 0.19 (0.13;0.27)	23/71 0.32 (0.22;0.45)	21/71 0.30 (0.19;0.42)	20/48 0.42 (0.28;0.57)
Humerus fracture PPV (95% CI)	224	9/224 0.04 (0.02;0.07)	8/169 0.05 (0.02;0.09)	NA NA	NA NA
Clinical vertebral fracture PPV (95% CI)	140	20/140 0.14 (0.09;0.21)	7/54 0.13 (0.05;0.25)	NA NA	NA NA
Wrist fracture PPV (95% CI)	177	13/177 0.07 (0.04;0.12)	12/97 0.12 (0.07;0.21)	NA NA	NA NA

Notes: *Admission date is the date the patient is admitted to the hospital for an inpatient contact and respectively, the date of visit for an outpatient contact.

Abbreviations: PPV, Positive Predictive Value; MOFs, Major Osteoporotic Fractures; NA, Not applicable as surgical procedures were only investigated for hip fractures.

improved from 0.69 (95% CI: 0.65;0.73) to 0.80 (95% CI: 0.76;0.83), in humerus fractures the PPV improved from 0.47 (95% CI: 0.43;0.52) to 0.54 (95% CI: 0.50;0.59), in clinical vertebral fractures the PPV improved from 0.47 (95% CI: 0.43;0.51) to 0.66 (95% CI: 0.61;0.72) and when applied to wrist fractures the PPV improved from 0.58 (95% CI: 0.54;0.62) to 0.72 (95% CI: 0.67;0.76). Specifically for hip fractures an additional criteria of a surgical procedure within

7 days of the fracture together with an imaging study improved the PPV from 0.69 (95% CI: 0.65;0.73) to 0.83 (95% CI: 0.79;0.86). The flow of the analysis is furthermore visualized in [Figure 1](#) with hip fractures as example ([Figure 1](#)).

Of the 1332 MOFs with identical dates in NPR and medical records, a total of 1266 was registered as 1st contacts. In analyses investigating 1st contacts, PPV increased compared to analyses above with PPV=0.73 (95% CI: 0.71;0.75) for MOF overall, PPV=0.83 (95% CI: 0.79;0.86) for hip fractures, PPV=0.73 (95% CI: 0.69;0.78) for humerus fracture, PPV=0.57 (95% CI: 0.53;0.62) for clinical vertebral fractures and PPV=0.79 (95% CI: 0.75;0.83) for wrist fractures. When applying criteria of procedural codes within +7 days of the fracture date PPV improved for all fracture sites. PPVs were PPV=0.88 (95% CI: 0.84;0.91) for hip fractures, PPV=0.78 (95% CI: 0.74;0.83) for humerus fractures, PPV=0.78 (95% CI: 0.73;0.83) for clinical vertebral fractures and PPV=0.87 (95% CI: 0.83;0.90) for wrist fractures. Analyses investigating ≥ 2 nd contacts of the 1332 (n=66) resulted in PPVs <0.50 for MOF overall and for the four individual fractures sites ([Table 3](#)). Analyses presented in [Table 3](#) were also performed stratified by primary and secondary diagnoses, however PPVs did not change (data not shown).

Additionally, in analyses investigating ≥ 2 nd contacts (n=66), PPVs improved when applying grace periods of 30, 60, 90 and 180 days between 1st and ≥ 2 nd fracture dates ([Table 4](#)). For hip and humerus fractures, the highest PPVs were detected when applying a 180 day grace period. In clinical vertebral and wrist fractures, the highest PPVs were detected with a 90 day grace period. However, sample sizes were small and CIs wide ([Table 4](#)).

Sensitivity Analyses

In supplementary analyses a $-7/+7$ days window was allowed to catch registrations of imaging studies and surgical procedures, which resulted in overall lower PPVs, indicating that the addition of the time window before the fracture date

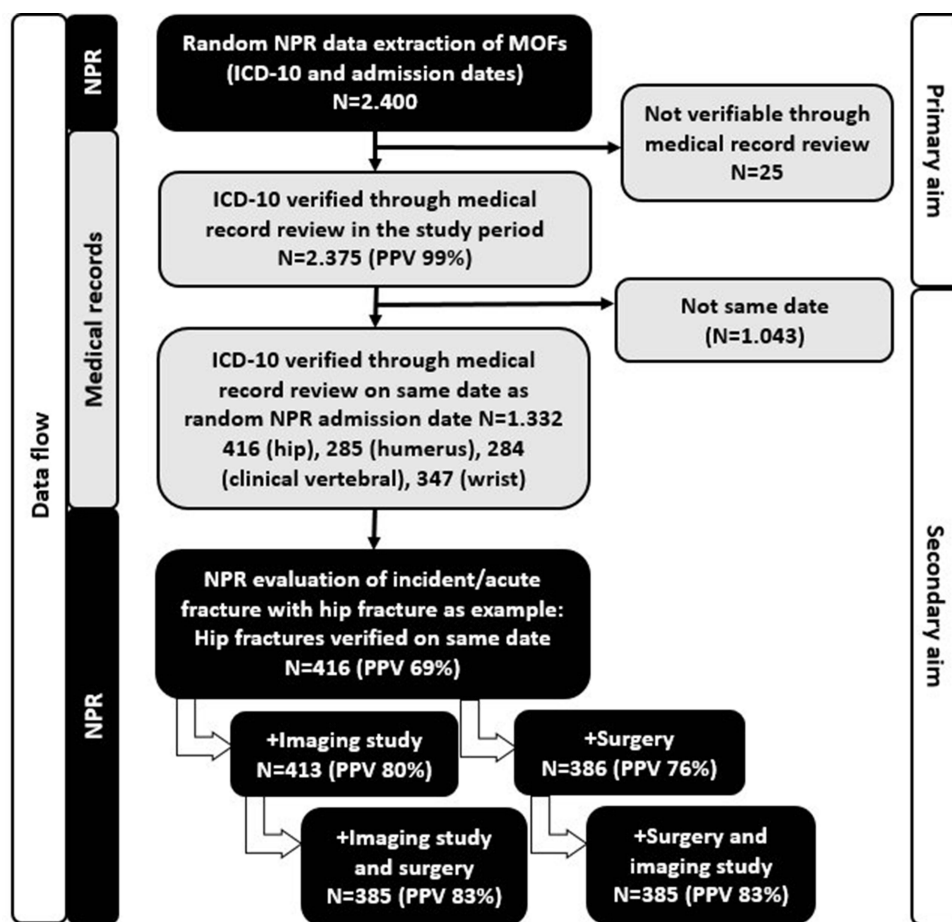


Figure 1 Flowchart of analysis approach.

Table 4 PPVs of ≥ 2 nd Admission Date* in the NPR with Grace Periods of 0, 30, 60, 90 and 180 Days

Diagnoses	Total ICD-10, N=667	Verified on Same Date, N / N Total	Verified on Same Date, N / N with ≥ 30 Days Between 1st and ≥ 2 nd Admission Date in NPR	Verified on Same Date, N / N with ≥ 60 Days Between 1st and ≥ 2 nd Admission Date in NPR	Verified on Same Date, N / N with ≥ 90 Days Between 1st and ≥ 2 nd Admission Date in NPR	Verified on Same Date, N / N with ≥ 180 Days Between 1st and ≥ 2 nd Admission Date in NPR
Hip Fracture PPV (95% CI)	126	24/126 0.19 (0.13;0.27)	13/38 0.34 (0.20;0.51)	13/29 0.45 (0.26;0.64)	13/24 0.54 (0.33;0.74)	7/12 0.58 (0.28;0.85)
Humerus fracture PPV (95% CI)	224	9/224 0.04 (0.02;0.07)	5/39 0.13 (0.04;0.27)	NR 0.17 (0.05;0.37)	NR 0.20 (0.06;0.44)	NR 0.30 (0.07;0.65)
Clinical vertebral fracture PPV (95% CI)	140	20/140 0.14 (0.09;0.21)	8/65 0.12 (0.05;0.23)	7/44 0.16 (0.07;0.30)	6/36 0.17 (0.06;0.33)	NR 0.12 (0.00;0.53)
Wrist fracture PPV (95% CI)	177	13/177 0.07 (0.04;0.12)	6/14 0.43 (0.18;0.71)	5/11 0.45 (0.17;0.77)	NR 0.50 (0.16;0.84)	NR 0.50 (0.12;0.88)

Note: *Admission date is the date patient is admitted to the hospital for an inpatients contact and respectively the date of visit for an outpatient contact.

Abbreviations: PPV, Positive Predictive; NR, Not reported due to small numbers.

added insecurity to results (Table S2). In a second supplemental analysis a -1 day grace period was allowed for the verification of fractures in medical records, meaning that the sample also included fractures that were verified in medical records on the day before the randomly extracted NPR fracture date (N=1546) which improved PPV results for all four fracture sites. The PPV improved most notably for hip fractures that resulted in PPV=0.96 (95% CI: 0.94;0.98) after inclusion of procedural codes (Table S3).

Discussion

Main Findings

This study verified 2375 of 2400 randomly extracted MOF diagnoses from the NPR through medical record review, resulting in a PPV of 99%. Of the 2375 verified MOFs, 1332 were verified in medical records on the same date as the randomly extracted NPR fracture date and were used for further analyses as they were considered to represent incident/acute fractures. In this analysis PPVs improved by combining diagnoses with a NPR registration of an imaging study (all fracture sites) and a surgical procedure (hip fractures only) within $+7$ days of the date of the diagnosis. PPVs improved further if the contact was the patients' 1st in the register with the fracture diagnoses. While some of these improvements of PPV are of limited magnitude, even a 5% improvement of PPV could meaningfully limit the number of false positive patients included in epidemiological studies. When introducing grace periods between fracture dates, PPVs improved when including patients in the sample with up until ≥ 90 days between the 1st and the ≥ 2 nd contact with the diagnosis in the register. This indicates that care is required when interpreting recurrent MOF registrations in the registers, as it is hard to distinguish between follow-up hospital visits and new fractures in administrative data. The findings from this study are relevant for future research in MOF, where cases are solely identified through ICD-10 codes within the NPR, as it shows that the ICD-10 codes are valid in detecting MOF in the NPR. Moreover, the findings of this study would also be relevant if administrative data would be used in screening or personalized medicine approaches in the future.

Comparison to Other Studies

Previous studies found similarly to this study high validity of fracture diagnoses in administrative data.^{14,17–20} Others investigated the validity of ICD-10 coded fracture diagnoses in the NPR,^{14,17,21} however this study is to our knowledge the first to investigate the validity of the specific ICD-10 codes chosen here to define MOF in the NPR. The data quality

and validity of diagnostic codes in the NPR was examined by Schmidt et al,¹¹ however they did not identify any studies examining the PPV of osteoporotic fractures. Furthermore, findings were that PPVs of reported diagnoses in the NPR ranged from <15% to 100%, proving large variation in data validity, underlining the need to perform validation studies when using NPR data. Additionally, this study is to our knowledge also the first to investigate definition of incident/acute fractures with date criteria, procedural codes and grace periods.

Karimi et al found an overall high PPV of 89.3% for humerus fractures in the NPR,¹⁷ supporting the results of our study where a PPV of 99% was found for humerus fractures. The difference in findings between the two studies may be explained by that Karimi et al used a wider ICD-10 definition.¹⁷

Hjelholt et al investigated the validity of ICD-10 hip fracture diagnoses in the NPR and found similarly to this study high PPVs with the same ICD-10 codes.¹⁴ Hjelholt et al also investigated the validity of procedural codes for hip surgical procedures,¹⁴ which improved our PPV results when applied to our analyses. These findings support that a hip fracture should be defined in the NPR with both a diagnosis and a surgical code. Further, studies from other country settings have investigated the validity of ICD-9 coded MOFs in administrative data and established overall high validity.^{18–20} Comparisons between these studies and our study is however not straightforward since these studies investigated ICD-9 coded MOFs (ICD-10 in our study) in different country-, administrative- and database settings. Nevertheless, when translating the ICD-9 codes into ICD-10 through a converter it seems that the codes mostly do overlap.^{18–20}

Earlier in this paper it was argued that some fractures could be misclassified as osteoporotic fractures which can be problematic for research purposes. Findings from a study by Martinez-Laguna et al however support that the fracture sites included in the MOF definition in our study can likely be characterized by fragility and possible osteoporosis as it was concluded that the majority of fractures from classic osteoporotic fracture sites was verified as fragility fractures (91.7% of hip fractures, 87.7% of spine fractures and 80.5% of major fractures (hip, spine, wrist/forearm and proximal humerus)).²²

Methodological Strengths and Limitations

A considerable methodological strength of this study is the large sample size of 2400 records for medical record review ensuring high statistical power. Another methodological strength is the application of an algorithmic search function as a state-of-the-art method for the identification of fracture descriptions in medical record text material. Additionally, it adds to the strength of the study that all identified text passages were reviewed by medical doctors and that an orthopedic surgeon was consulted in cases of doubt. Furthermore, it must be considered a methodological strength that we accounted for the possible delay between administrative systems in sensitivity analyses by allowing a –1 day grace period. The idea is that the fracture could possibly be registered in the medical record system 1 day before the fracture is registered in the NPR due to delay between the two systems. This suspicion was confirmed in [Table S3](#) which proved to identify 214 additional fractures in the entire sample by allowing contacts from medical records that occurred the day before the fracture date obtained from the NPR. This finding is however not useful in NPR definitions of MOF, unless researchers have access to medical record data, and it was therefore not included in the conclusion.

Our study also had some methodological limitations to consider. Firstly, the validation performed in this study was done on the group level as each fracture site was defined by a set of ICD-10 codes which could possibly have added insecurity to results. Secondly, even though the MOF concept implies that fractures are caused by osteoporosis or low energy trauma we cannot ascertain this with ICD-10 codes alone as the underlying mechanisms are not investigated. Thirdly, it is a possible limitation that our data extraction only included patients from the Region of Southern Denmark (Denmark consists of 5 administrative regions, each responsible for managing the regional healthcare system). However, Henriksen et al concluded that the five Danish regions were overall similar with regard to sociodemographic and health related characteristics and that studies conducted in regional data samples have a high degree of generalizability.²³ Furthermore, the results of this study are based on data from the Danish National Patient Register, which directly receives data from all Danish public hospitals. Other countries may not have an equally comprehensive registry, and the findings of this study may not be directly applicable to them. Hence, separate validation studies, possibly with a methodology similar to our current study, within the specific registries of other countries is needed to assess generalizability.

Conclusion

In conclusion, ICD-10 coded MOF diagnoses are valid in the NPR with a PPV of 99%. The four individual fracture sites (hip, humerus, clinical vertebral and wrist) resulted in a PPV of 99% for each individual fracture site, respectively. Furthermore, we conclude that a set of criteria can be applied to assure that MOF registrations in the NPR represent incident/ acute fractures. Firstly, a MOF diagnosis and its' date should be combined with NPR registrations of imaging studies within +7 days. Specifically for hip fractures, an additional criteria of a NPR registration of a surgical procedure together with an imaging study should be applied within a +7 day window of the date of the fracture. Secondly, the patients' first contact date with the diagnoses should be used to define the incident fracture. Thirdly, a grace period of at least 90 days should be introduced between fracture contacts to qualify that the fracture is incident/acute.

Data Sharing Statement

Data is not available for publication as it contains personal identifiers. Data was stored at a secure server hosted at the Danish Health Data Authority.

Ethics Statement

The medical record review was approved by The Regional Council of the Region of Southern Denmark (journal number: 22/13638) and by the department heads of the involved departments at the included hospitals. The study was not a clinical trial. The researchers did at no point contact or in any other ways interact with the patients. The study complies with the Declaration of Helsinki.²⁴

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Disclosure

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References

1. Compston JE, McClung MR, Leslie WD. Osteoporosis. *Lancet*. 2019;393(10169):364–376. doi:10.1016/S0140-6736(18)32112-3
2. Leslie WD, Schousboe JT, Morin SN, et al. Fracture risk following high-trauma versus low-trauma fracture: a registry-based cohort study. *Osteoporos Int*. 2020;31(6):1059–1067. doi:10.1007/s00198-019-05274-2
3. Briot K, Paternotte S, Kolta S, et al. FRAX®: prediction of major osteoporotic fractures in women from the general population: the OPUS study. *PLoS One*. 2013;8(12):e83436. doi:10.1371/journal.pone.0083436
4. Clausen A, Möller S, Skjødt MK, Bech BH, Rubin KH. Evaluating the performance of the Charlson Comorbidity Index (CCI) in fracture risk prediction and developing a new Charlson Fracture Index (CFI): a register-based cohort study. *Osteoporos Int*. 2022;33(3):549–561. doi:10.1007/s00198-021-06293-8
5. Rubin KH, Möller S, Holmberg T, Bliddal M, Søndergaard J, Abrahamsen B. A New Fracture Risk Assessment Tool (FREM) Based on Public Health Registries. *J Bone Miner Res*. 2018;33(11):1967–1979. doi:10.1002/jbmr.3528
6. Skjødt MK, Möller S, Hyldig N, et al. Validation of the Fracture Risk Evaluation Model (FREM) in predicting major osteoporotic fractures and Hip fractures using administrative health data. *Bone*. 2021;147:115934. doi:10.1016/j.bone.2021.115934
7. Berry SD, Samelson EJ, Pencina MJ, et al. Repeat bone mineral density screening and prediction of Hip and major osteoporotic fracture. *JAMA*. 2013;310(12):1256–1262. doi:10.1001/jama.2013.277817

8. Looker AC. Serum 25-hydroxyvitamin D and risk of major osteoporotic fractures in older U.S. adults. *J Bone Miner Res*. 2013;28(5):997–1006. doi:10.1002/jbmr.1828
9. World Health Organization. International Statistical Classification of Diseases and Related Health Problems (ICD); 2022. Available from: <https://www.who.int/standards/classifications/classification-of-diseases>. Accessed March 27, 2024.
10. Konstantelos N, Rzepka AM, Burden AM, et al. Fracture definitions in observational osteoporosis drug effects studies that leverage healthcare administrative (claims) data: a scoping review. *Osteoporos Int*. 2022;33(9):1837–1844. doi:10.1007/s00198-022-06395-x
11. Schmidt M, Schmidt SA, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol*. 2015;7:449–490. doi:10.2147/CLEP.S91125
12. Laursen MS, Pedersen JS, Vinholt PJ, Hansen RS, Savarimuthu TR. Benchmark for evaluation of Danish clinical word embeddings. *North Eur J Lang Technol*. 2023;9(1). doi:10.3384/nejlt.2000-1533.2023.4132
13. Pedersen JS, Laursen MS, Rajeeth Savarimuthu T, et al. Deep learning detects and visualizes bleeding events in electronic health records. *Res Pract Thromb Haemost*. 2021;5(4):e12505. doi:10.1002/rth2.12505
14. Hjelholt TJ, Edwards NM, Vesterager JD, Kristensen PK, Pedersen AB. The positive predictive value of Hip fracture diagnoses and surgical procedure codes in the Danish multidisciplinary Hip fracture registry and the Danish National Patient Registry. *Clin Epidemiol*. 2020;12:123–131. doi:10.2147/CLEP.S238722
15. StataCorp. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LLC; 2021.
16. StataCorp. *Stata Statistical Software: Release 18*. College Station, TX: StataCorp LLC; 2023.
17. Karimi D, Houkjær L, Gundtoft P, Brorson S, Viberg B. Positive predictive value of humeral fractures in the Danish National Patient Registry. *Dan Med J*. 2023;70(4):A10220612.
18. Sing CW, Woo YC, Lee ACH, et al. Validity of major osteoporotic fracture diagnosis codes in the Clinical Data Analysis and Reporting System in Hong Kong. *Pharmacoepidemiol Drug Saf*. 2017;26(8):973–976. doi:10.1002/pds.4208
19. Jean S, Candas B, Belzile É, et al. Algorithms can be used to identify fragility fracture cases in physician-claims databases. *Osteoporos Int*. 2012;23(2):483–501. doi:10.1007/s00198-011-1559-4
20. Wright NC, Daigle SG, Melton ME, Delzell ES, Balasubramanian A, Curtis JR. The Design and Validation of a New Algorithm to Identify Incident Fractures in Administrative Claims Data. *J Bone Miner Res*. 2019;34(10):1798–1807. doi:10.1002/jbmr.3807
21. Gundtoft PH, Danielsson FB, Houllind M, et al. The positive predictive value of ankle fracture diagnosis in the Danish National Patient Registry. *Dan Med J*. 2022;69(12):A01220032.
22. Martinez-Laguna D, Soria-Castro A, Carbonell-Abella C, et al. Validation of fragility fractures in primary care electronic medical records: a population-based study. *Reumatol Clin*. 2019;15(5):e1–e4. doi:10.1016/j.reuma.2017.10.013
23. Henriksen DP, Rasmussen L, Hansen MR, Hallas J, Pottegård A, Dalal K. Comparison of the five Danish regions regarding demographic characteristics, healthcare utilization, and medication use--a descriptive cross-sectional study. *PLoS One*. 2015;10(10):e0140197. doi:10.1371/journal.pone.0140197
24. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191–2194. doi:10.1001/jama.2013.281053

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