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**IMPACT OF UK NATIONAL GUIDELINES BASED ON FRAX® -
COMPARISON WITH CURRENT CLINICAL PRACTICE**

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IMPACT OF UK NATIONAL GUIDELINES BASED ON FRAX[®] - COMPARISON WITH CURRENT CLINICAL PRACTICE

Short title: Impact of FRAX[®]

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Key Words: FRAX[®]; NOGG; osteoporosis; fracture

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ABSTRACT:

Objective: To assess whether clinician-determined treatment intervention thresholds are in line with the assessment of fracture risk provided by FRAX[®] and treatment recommendations provided by UK guidelines produced by the National Osteoporosis Guidelines Group (NOGG).

Design, Patients and Measurements: This was a retrospective cohort analysis of 288 patients consecutively referred for DXA scanning from primary care immediately prior to the introduction of the FRAX[®] algorithm. In addition to DXA assessment, patients completed a clinical risk factor questionnaire which included risk factors used in the FRAX[®] algorithm. Initial risk assessment and treatment decisions were performed after DXA. FRAX[®] was used, retrospectively, with femoral neck T-score, to estimate fracture risk which was applied to NOGG to generate guidance on treatment intervention. Clinician- and NOGG-determined outcomes were audited for concordance.

Results: There was concordance between clinician and NOGG treatment decisions in 210 (72.9%) subjects. Discordance was observed in 78 (27.1%) subjects. In the discordant group, 7 subjects were given lifestyle advice when NOGG recommended treatment, 41 given treatment when NOGG recommended lifestyle advice only, and 30 were referred to a metabolic bone clinic for further evaluation. The reasons for treatment differences in subjects recommended treatment by clinician but not NOGG were largely (90.2%) due to use of lumbar spine BMD.

Conclusions: There is high concordance between clinician-determined and FRAX[®]-NOGG intervention. The absence of spine BMD from FRAX[®] is the primary source of discrepancy. This study provides some assurance of the validity of the treatment thresholds generated from FRAX[®]-NOGG in 'real-world' usage.

INTRODUCTION:

Decisions regarding who should receive treatment for osteoporosis are based on a range of factors. Since the World Health Organisation (WHO) introduced an operational definition of osteoporosis based on dual-energy x-ray absorptiometry (DXA)-determined T-scores, decisions for treatment have relied heavily on this measure¹². More recently the importance of additional risk factors such as age and prior fractures have been emphasised and this has been incorporated into some clinical guidelines (e.g. National Institute for Health and Clinical Excellence (NICE) Osteoporosis Technology Appraisals¹) or been used in a more subjective way by specialists to rationalise approaches to treatment. The introduction of the FRAX[®] algorithm⁷ has resulted in a more robust way to estimate fracture risk although this still has some limitations, including the ability to adjust for some aspects of individual patient risk e.g. number of fractures or dose and duration of glucocorticoid treatment. In the UK an advisory group, the National Osteoporosis Guidelines Group (NOGG), have linked the output scores obtained with FRAX[®] to guidance on who to investigate with DXA and who to treat without the requirement for prior DXA⁸. **The aims of NOGG are to provide assessment thresholds for the use of BMD i.e. the fracture probabilities at which a BMD test might or might not be recommended, and to provide FRAX[®] based intervention thresholds, based on the existing UK case-finding strategy.** The aim of this retrospective study was to assess whether clinician-determined treatment intervention thresholds (not using FRAX[®]-NOGG) were in line with the objective assessment of fracture risk provided by FRAX[®] and treatment intervention thresholds provided by UK guidelines produced by the NOGG.

METHODS:

The study took place between April 2008 and September 2008 and 288 patients consecutively referred for DXA scanning from a primary care setting were included. The demographic details for these patients are shown in table 1. An outline schema of the patient assessment is shown in figure 1. Standard DXA assessment was performed at the hip and spine using a Lunar Prodigy scanner. Patients also completed a clinical risk factor questionnaire that has been in routine use within the unit for several years and included pertinent risk factors used to populate the FRAX[®] algorithm. This self completed questionnaire asked for details of previous fractures, height loss, parental history of fracture, glucocorticoid use, age at menopause, HRT use and tobacco consumption. Initial risk

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3 assessment and treatment decisions were performed shortly after the time of DXA scan
4 taking into account the DXA results, information provided by the patient questionnaire and
5 information provided on the patient referral letter e.g. previous medical history, current and
6 previous medication use. Clinical decisions were made by a consultant physician, 3 of whom
7 were involved with the study. The basis for the clinical decisions made by the consultants
8 was not studied systematically here (except where clinical decisions and those indicated by
9 FRAX[®]-NOGG differed) but it would be anticipated that these decisions would be strongly
10 influenced by the UK guidelines available at the time of the study which included the Royal
11 College of Physicians UK guidance from 1999 and those from NICE^{1,10,11}.
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21 Initially the FRAX[®]-NOGG guidelines were used to determine whether referral for DXA
22 was warranted initially on the basis of clinical risk factors alone. The FRAX[®] tool was then
23 used, retrospectively, in conjunction with femoral neck bone mineral density (BMD) T-
24 score, to estimate fracture risk which was subsequently applied to NOGG to generate
25 guidance on treatment intervention. Clinician- and NOGG-determined outcomes were
26 audited for concordance.
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33 **RESULTS:**

34 **Concordance for recommendations for DXA:**

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36 The concordance of recommendations for DXA measurement by FRAX[®] in those patients
37 actually referred for DXA scanning is shown in figure 2A. In only 53% of patients actually
38 referred did FRAX[®]-NOGG guidance suggest referral for DXA. In 5% of patients NOGG
39 guidance would have suggested treatment without the need for DXA. In 41% of patients
40 NOGG guidance indicated lifestyle advice alone. The reasons for referral where NOGG
41 guidance would have indicated lifestyle advice alone are shown in figure 2B. The majority
42 of these patients were referred with an accepted risk factor for osteoporosis that is not
43 incorporated into the FRAX algorithm (osteopaenia on radiograph n=36 family history of
44 non-hip fracture(s) n=36 height loss/kyphosis n=11). A small number of patients (n=12)
45 were referred for decisions relating to the continuing use of HRT that had been started due to
46 early menopause. In the remaining 24 patients (7% of total population) one or more risk
47 factors included in FRAX[®] were present.
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Concordance for recommendations for treatment with DXA results available:

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3 The concordance of recommendations for treatment based on clinician evaluation of all
4 available information and recommendations based on the FRAX[®]-NOGG guidance are
5 shown in figure 3A. There was concordance between clinician and NOGG on treatment
6 decision in 210 (72.9%) subjects. A breakdown of the concordant treatment decisions is
7 given in figure 3B. Discordance was observed in 78 (27.1%) subjects. In the discordant
8 group, 7 subjects were given lifestyle advice when NOGG recommended treatment, 41 were
9 given treatment when NOGG recommended lifestyle advice only, and 30 were referred to a
10 metabolic bone clinic for further evaluation. The reasons for treatment differences are shown
11 in figure 4 and table 2. The primary reason for lifestyle advice when NOGG recommended
12 treatment was the absence of osteoporosis determined by DXA (**table 2A**). The reason for
13 recommendation of active treatment by clinician but not FRAX[®]-NOGG guidance was
14 primarily (37/42 patients) due to the presence of spinal osteoporosis. In the remaining 5/42
15 patients the contributing factors that suggested treatment are outlined in table 2B. The
16 reasons for discordant decisions made after patients were seen in the metabolic bone clinic
17 are shown in table 2C. These were all treatment recommendations by physician when NOGG
18 suggested lifestyle and comprised of patients who had either isolated osteoporosis at the
19 spine or had low bone density in the presence of vertebral fractures (some only identified on
20 further investigation).

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37 **Concordance of decisions made using FRAX[®]-NOGG without BMD and ultimate**
38 **clinical decisions with BMD available:**

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40 **119 of the individuals referred for DXA in this study would have been recommended**
41 **lifestyle advice alone using FRAX[®]-NOGG guidance (figure 2A). Of these 119**
42 **individuals 103 were ultimately recommended lifestyle advice alone and 16 were**
43 **recommended treatment. 15 individuals would have been recommended treatment**
44 **without using FRAX[®]-NOGG. Of these 15 individuals 11 were ultimately**
45 **recommended for treatment.**
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DISCUSSION:

We retrospectively examined the concordance of decisions actually made by experienced osteoporosis physicians without the use of FRAX[®] and/or NOGG guidelines and decisions that would have been made if FRAX[®]-NOGG recommendations had been used in isolation. We found that the majority of patients referred for bone densitometry would have been referred for densitometry using FRAX[®]-NOGG guidelines. The main reason for referral when FRAX[®]-NOGG guidance suggested no treatment/referral was the presence of indications for DXA assessment based on previous guidelines (primarily the Royal College of Physicians guidelines^{10,11}). Indications such as osteopaenia on radiographs and a family history of low trauma fractures appear valid indications for densitometry even though they were not able to be incorporated into FRAX[®]-NOGG. There was also a high rate of concordance between treatment decisions made by clinicians without the use of FRAX[®]-NOGG and decisions that would have been made if based solely on FRAX[®]-NOGG. The commonest reason by far for discordance in decisions was where active treatment was recommended by a clinician on the basis of low bone density at the spine, information which is not incorporated into the FRAX[®]-NOGG.

A likely reason for the high degree of concordance between experienced clinicians' judgements from UK based specialists and FRAX[®]-NOGG is that the intervention thresholds for NOGG were determined to try to maintain approximate equivalence with previous UK guidelines. This study suggests that this attempt to establish equivalence has been a success. This probably explains why the physicians appeared to incorporate some clinical risk factors (particularly previous fracture, something emphasised by both Royal College and NICE guidance) in their recommendations in contrast to the findings from a recent Canadian study². However, these previous guidelines did not place a central emphasis on hip BMD in contrast to the output of FRAX[®]-NOGG and this appeared to be the main reason for discordance (both where recommendations were based on patient information/DXA alone and after attendance at the metabolic bone clinic). An important issue that arises from this study is what to do in the setting of discordant BMD at hip and spine where spine BMD is substantially lower than that of the hip. A proportion of patients in the pivotal randomised trials on which most of the data relating to treatments have been derived had this pattern of bone loss and patients appeared to have a beneficial effect of treatment^{6,9}. Many health economic models place much less emphasis on the consequences of vertebral fractures

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3 (especially morphometric fractures) due to their lower direct cost. However, **it is now clear**
4 **that vertebral fractures are themselves associated with increased mortality**³⁻⁵. In clinical
5 practice it would **thus** appear impossible to totally discount information regarding such a
6 high, treatable, fracture risk, so many of these patients are likely to continue to be treated.
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12 The other situations where there was discordance in recommendations were also interesting.
13 Recommendations for lifestyle advice alone by physician when NOGG indicated treatment
14 appeared to be explained entirely by the absence of osteoporosis on DXA scanning despite
15 the presence of a high fracture risk. The recommendations for lifestyle advice are probably
16 explained by the emphasis on a DXA based diagnosis of osteoporosis intrinsic in previous
17 WHO guidelines and more lately RCP and NICE guidelines. There is also the additional
18 issue of whether bisphosphonates are effective at reducing fracture risk in individuals who
19 have normal BMD. This is an important area of current debate. Our data do however suggest
20 that the overall number of patients where this issue arises is relatively small.
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30 There are a number of limitations to our study. This approach was unable to determine the
31 full potential impact of FRAX[®]-NOGG on referrals for densitometry. We are only able to
32 evaluate patients who have been referred who might not have been, based on FRAX[®]-
33 NOGG. We are clearly unable to assess the population of patients who should have been
34 referred for DXA on the basis of FRAX[®]-NOGG but were not, or the population that were
35 given treatment without recourse for DXA who may or may not have been recommended for
36 treatment on FRAX[®]-NOGG. In this particular health setting, where utilisation of DXA and
37 anti-osteoporosis medications is relatively low, it is likely that there are many patients being
38 seen in primary care who would be recommended for treatment/evaluation by FRAX[®]-
39 NOGG. There was also an inflexible approach used to the FRAX[®]-NOGG guidance. It is
40 stated explicitly in this guidance that there are many situations where fracture risk will be
41 underestimated e.g. patients with clinical vertebral fractures or multiple fractures. A more
42 flexible interpretation of these guidelines, as would be likely in clinical practice, would
43 almost certainly have reduced further some of the discordance between decisions. **It should**
44 **also be noted that the NOGG guidelines suggest that postmenopausal women with a**
45 **prior fragility fracture can be treated without FRAX assessment although BMD**
46 **assessment may be appropriate. We decided not to apply this criteria in our study as**
47 **use of the FRAX[®]-NOGG algorithm does not always lead to a decision to treat in these**
48 **patients and there would have been ambiguity regarding when BMD assessment would**
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4 **be appropriate. If we had taken this more literal interpretation of the NOGG guidance**
5 **then 3 of the 12 treatment discordant patients in tables 2B and 2B would have been**
6 **reclassified as concordant.**
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10 This study illustrates that the concordance between decisions that were made by a group of
11 UK physicians before the introduction of the FRAX[®] algorithm and UK based NOGG
12 guidance and those that would have been made using this guidance was high. It also
13 highlights the reasons for discordant advice which were primarily the additional use of bone
14 density results for the spine (leading to more treatment than recommended by NOGG) and
15 the withholding of treatment by physicians in patients with high fracture risk but lacking
16 osteoporosis by densitometric criteria.
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Table 1: Demographic details of the patients included in this study (mean \pm SD or % of cohort of 288 subjects: FN; femoral neck; RA; rheumatoid arthritis):

Female (%)	88.5
Age (years)	63 \pm 11
BMI (kg/m ²)	27 \pm 5
Previous # (%)	37
FN T score	-1.2 \pm 1.1
Steroid ever (%)	13
RA history (%)	2

For Peer Review

Table 2: Details of patients discordant for treatment decisions (see figure 4):**A. Decision life-style advice when FRAX[®]-NOGG guidance suggested treat**

Gender (F=female)	Age (Years)	Hip BMD T-score	Spine BMD T-score	Additional information (FN T: femoral neck T score)
F	55	-0.9	-1.2	FH hip #, alcohol use, FN T -1.4
F	62	0.8	2.8	Prior #, FH hip #, FN T 0.0
F	52	-1.3	-0.4	Prior #, alcohol use, prior steroids
F	61	-1.6	-2.1	Prior #, FH hip #
F	64	0.4	-0.5	Prior #, FH hip #, FN T -0.3
F	50	-2.0	-1.6	Prior #, alcohol use
F	51	-1.4	-1.9	Prior #, alcohol use

**B. Physician decision treat when FRAX[®]-NOGG guidance suggested lifestyle advice
(for 37 additional patients treatment given on basis of spine osteoporosis)**

Gender (F=female)	Age (Years)	Hip BMD T-score	Spine BMD T-score	Additional information
F	72	-0.5	-1.8	4 years treatment with alendronate
F	81	-2.1	-2.0	Difficult spine study ?osteoporosis
F	59	-2.8	-1.5	Family history of non-hip #s
F	69	0.2	-1.1	Clinical vert #, freq steroids courses
M	82	-2.2	-0.3	# hip, kyphosis

**C. Discordant treatment decisions in metabolic bone clinic (all physician
recommendations for treatment when FRAX[®]-NOGG guidance suggested lifestyle)**

Gender (F=female)	Age (Years)	Hip BMD T-score	Spine BMD T-score	Fractures present?
F	77	-1.8	-4.6	No
F	50	-2.1	-3.0	No
F	70	-0.7	-1.7	Yes, 2 clinical vertebral
F	76	-2.2	-1.7	Yes, multiple morphometric vertebral
F	56	-0.7	-1.5	Yes, 1 morphometric vertebral
F	76	-2.8	-4.5	No
F	50	-1.7	-2.8	No

LEGEND TO FIGURES:

Figure 1: *Schema illustrating the structure of the audit:*

There were 2 questions audited in this study. Firstly, the concordance of actual referral indications for our unit and those of FRAX[®]-NOGG for 288 patients involved in this study. Secondly, the concordance of clinician determined treatment recommendations with guidelines by FRAX[®]-NOGG. CRFs, clinical risk factors.

Figure 2: *Application of FRAX[®]-NOGG guidance without the availability of DXA information in patients actually referred for DXA:*

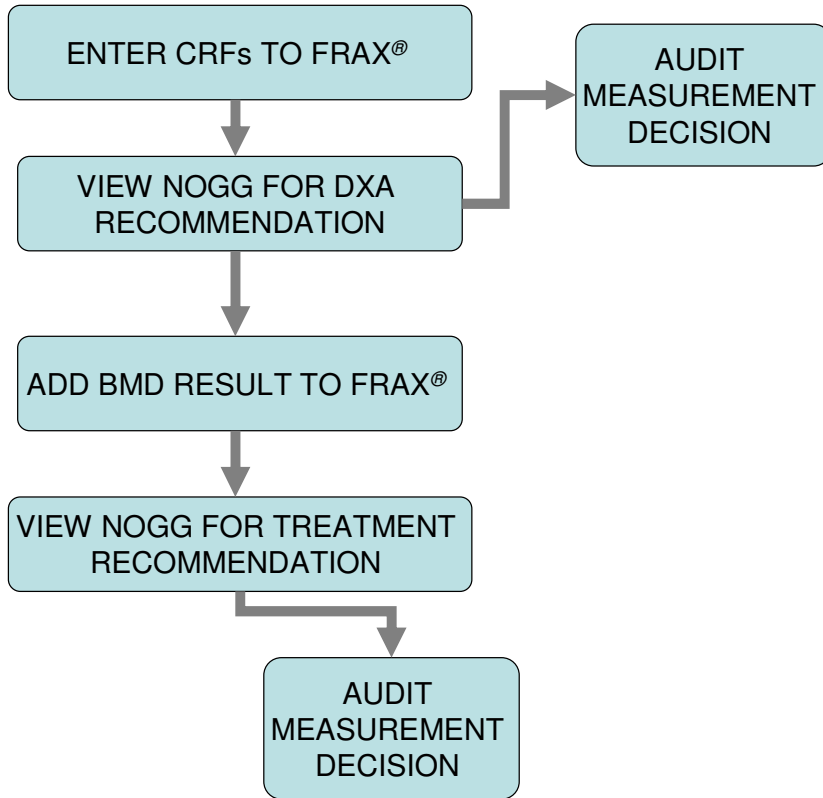
A. Number of patients concordant/discordant for FRAX[®]-NOGG recommendations. B. Breakdown of reasons for discordance where referral was made by a clinician but would not have been based on FRAX[®]-NOGG. Treated menopause refers to individuals treated with HRT for an early menopause where decisions regarding continuing use were needed.

Figure 3: *Concordance of intervention decisions made by experienced clinician and those recommended by FRAX[®]-NOGG guidance with DXA information available:*

Concordance for decisions is shown in A. B. Breakdown of recommendations for treatment in patients where there was concordance for treatment.

Figure 4: *Reasons for discordant recommendations by experienced clinician and FRAX[®]-NOGG guidance*

Figure 1:

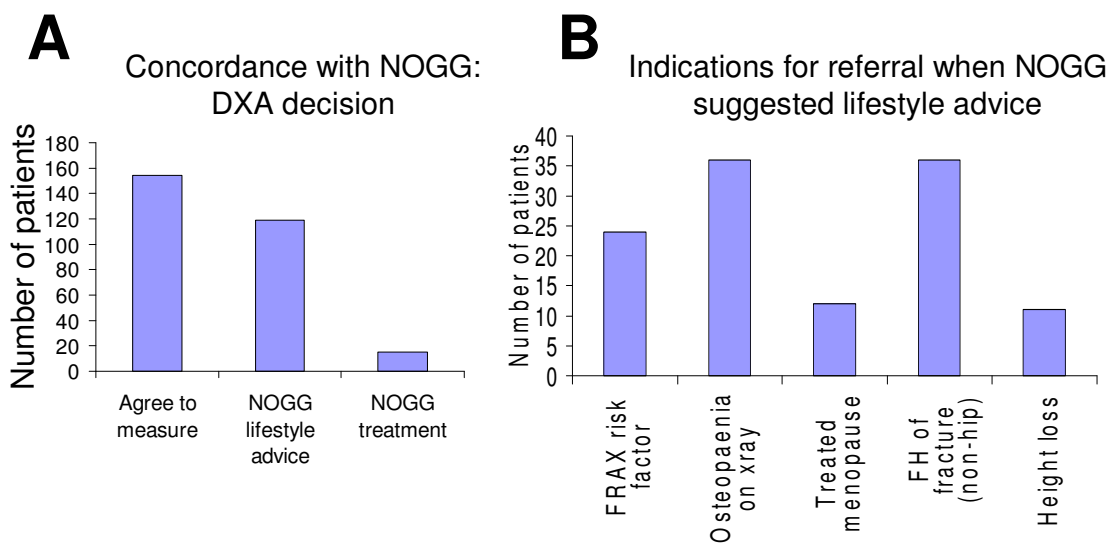


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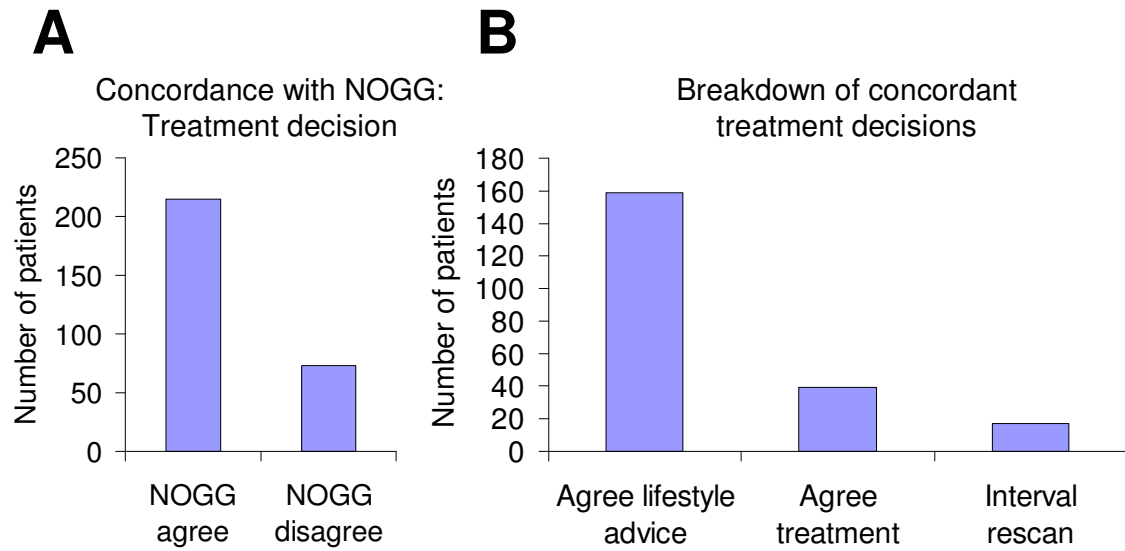
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Figure 2:



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Figure 3:

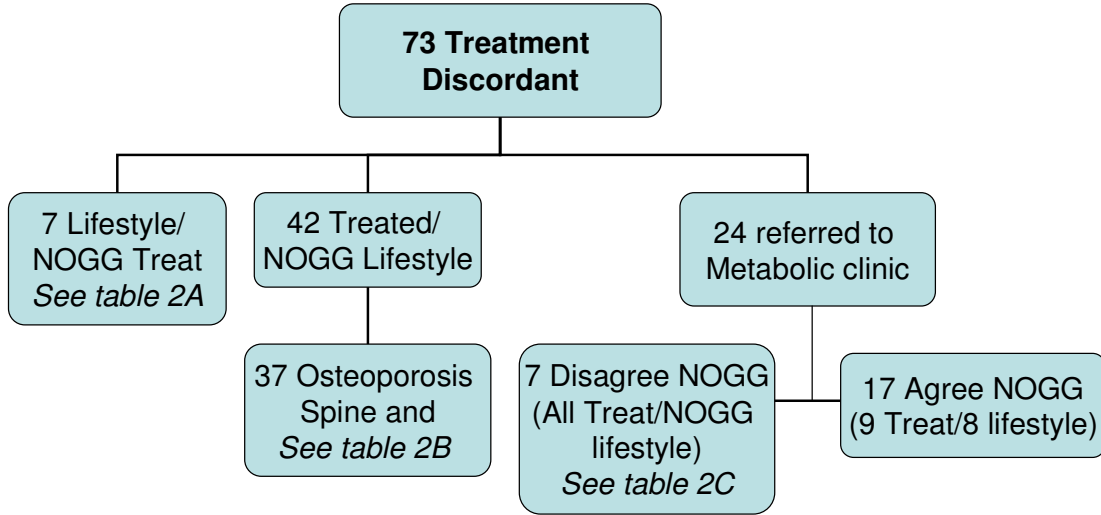


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Figure 4:



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