Vitamin D, bone mineral density and risk of fracture in people with intellectual disabilities

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Abstract

Background
People with intellectual disabilities (ID) have very high osteoporosis and fractures rates, to which their widespread vitamin D deficiency and other factors could contribute.
We aimed to assess in ID people previously treated for vitamin D deficiency 1) long-term adherence to vitamin D supplementation and 2) bone mineral density (BMD), as an indicator for risk of fractures, according to vitamin D supplementation and other factors.

Method
Height, weight, medical, pharmacological, dietary and lifestyle assessment; blood sample for vitamin D and related analytes; Dual-energy X-ray Absorptiometry (DXA) for BMD.

Results
Of 51 study participants (mean [SD] age 51.5 [13.6] years, 57 % male), 41 (80.4%) were taking vitamin D and 10 were not. Mean [SD] serum vitamin D was 81.3 [21.3] vs 25.2 [10.2] nmol/L ($p<0.0001$) respectively.
Thirty-six participants underwent a DXA scan, which showed osteoporosis in 23.7% and osteopenia in 52.6%.
Participants on vitamin D had higher BMD than those who were not, a statistically significant difference when confounders (lack of mobility, hypogonadism) were removed.
BMD was significantly different according to mobility, particularly in wheelchair users, in whom hip BMD was 33% lower ($p<0.0001$) than in participants with normal mobility.
Participants still taking vitamin D showed a 6.1% increase in BMD at the spine ($p=0.003$) after mean [SD] 7.4 [1.5] years vitamin D treatment.

Conclusions
In people with intellectual disabilities and previous vitamin D deficiency, bone mineral density increases on long-term vitamin D supplementation. However, additional strategies must be considered for osteoporosis and fracture prevention in this population.

Key words: intellectual disabilities; vitamin D; bone mineral density; osteoporosis; fracture; hypogonadism; impaired mobility

Background

People with intellectual disabilities (ID) have a high rate of osteoporosis and fractures. This is up to three times the rate of the general population (Balogh et al 2017; Vanlint and Nugent, 2006; Schrager S et al, 2007; Lohiya et al, 1999; Tannenbaum et al, 1989). They also have a very high prevalence of vitamin D deficiency (Vanlint and Nugent, 2006; Frighi et al, 2014; Chester et al, 2017; Kilpinen-Loisa, 2009), which could partly explain the bone findings (Holick, 2007). However, beside vitamin D deficiency, additional risk factors for osteoporosis and fractures, e.g. treatment with antiepileptic medication, hypogonadism, impaired mobility, are highly prevalent in the ID population (Srikanth et al, 2011; Hawli et al, 2009; Center et al, 1998). Previous studies, including eighteen meta-analyses or systematic reviews on the effects of vitamin D treatment with or without calcium on fracture prevention have led to conflicting results (Zhao et al, 2017; Avenell et al, 2014). However, most studies did not include measurements of serum vitamin D and long-term compliance with vitamin D treatment was generally poor. To our knowledge no studies either included let alone specifically focussed on people with intellectual disabilities.

The primary aim of this study was assessment of adherence to long-term vitamin D supplementation in people with ID who had been previously diagnosed with and treated for vitamin D deficiency. Our secondary aim was to assess bone mineral density (BMD), as an indicator for fracture risk (Marshall et al, 1996), in relation to vitamin D supplementation and other factors that may influence it such as age, gender, degree of mobility, body mass index, use of antiepileptic medication.

Methods

Ethics

The study was approved by the South Central- Oxford A Ethics Committee (REC 16/SC/0223). Capacity was assessed as outlined in section 4 of the Mental Capacity Act 2005 Code of Practice. We used pictures and easy read material to assess each person's understanding, we spoke to family and carers who knew the person and could support them to comprehend the information, we conducted the assessment in their homes where they were less likely to become anxious, hence more likely to understand information. People who had capacity gave written informed consent after explanation of the study. This was aided by a participant pictorial information sheet in a format which was accessible to people with a mild-to-moderate ID. For incapacitous participants, a personal consultee was identified whenever possible. In the lack of a relative or close friend that could fulfil this role, a nominated consultee was identified. This was either the person's carer or the GP. Explanation of the study was given with the aid of a consultee information pack. Incapacitous participants were recruited to the study only after their consultees had signed the declaration form. Informed consent by capacitous participants and declaration of "no objection" by consultees of incapacitous participants was obtained for study procedures and for accessing previous relevant biochemical and radiological data.

Type of study

Observational, cohort based study

Participants

People with ID who had been diagnosed with vitamin D deficiency and treated with vitamin D supplements in a good clinical practice initiative that was carried out in the Oxfordshire Learning Disabilities Trust in the years 2008-2011 (Frighi et al, 2014). Of the 81 original participants, 51 were recruited. Of the 30 people who were not included, seven had died, eleven had moved out of area, two were excluded (one because of oral steroid treatment and the other because of advanced stage cancer), four refused, and for another six people, their relatives or carers refused.

Study procedures

Participants were seen at a domiciliary visit by the study nurse with or without the principal investigator. A medical and drug history were taken, height and weight were measured for calculation of body mass index (BMI), and a blood sample was collected for 25(OH) D (vitamin D), calcium, phosphate, albumin and creatinine. An assessment was made of calcium intake, exposure to sunlight and degree of mobility with the help of a detailed questionnaire designed for the studyand administered to each participant's carer during the home visit. Average daily calcium intake was assessed via estimating the quantity of calcium-rich foods each participant was taking, based on the known calcium content of these foods. Exposure to sunlight was assessed by estimating the daily average amount of time spent outdoors by each participant during the period 1st April-30th September between 11 am and 3 pm, i.e. when UVB light can trigger the formation of vitamin D in the skin at UK latitude. A question was also asked about the use of sunscreen. Degree of mobility was categorised according to the participant's ability to walk 100 yards unaided (normal), having difficulties and requiring help to do so (limited) or by the need of a wheelchair (wheelchair user). Published instruments and literature were used to construct the questionnaire (International Osteoporosis Federation, 2017; Scientific Advisory Committee on Nutrition, 2007; Burke et al, 2017).

Biochemical analyses

Serum 25(OH) D was measured using a routine in-house immunoassay method. In line with current recommendations (National Institute for Health and Care Excellence, 2016; National Osteoporosis Society, 2013; Sai et al, 2011), our laboratory used a 25(OH) D threshold of >50 nmol/L for adequate vitamin D for bone health, with deficiency defined as 30-50 nmol/L, and severe vitamin D deficiency as <30 nmol/L. Calcium was measured by arsenazo III, phosphate by phosphomolybdate, albumin by bromocresol purple, and creatinine by enzymatic method on Abbott Arhitect autoanalysers.

Bone mineral density (BMD) measurements

These were carried out at the Nuffield Orthopaedic Centre in Oxford by dual-energy X-ray absorptiometry (DXA) on a Hologic scanner. As per standard procedures, measurements were taken at the lumbar spine, total hip and femoral neck and results expressed in g/cm2, in *t*-scores (number of standard deviations below the mean BMD of the general population of age 30 years), and in *z*-scores (number of standard deviations below the mean BMD of the general population of the same age and gender as the participant) for each anatomical site examined. Standard cutoff values were used for the definition of osteoporosis ($t \leq -2.5$) and osteopenia ($t = -1.1$ to -2.4).

Statistical analyses

Data were analysed using IBM SPSS (version 22) for Windows. The percentage of participants currently taking vitamin D supplements was calculated. Mean serum 25(OH) D levels were compared between people taking vitamin D supplements and those not taking any by independent samples t-test. Mean 25(OH) D levels were also compared with the 25(OH) D levels which had been found when vitamin D deficiency had been initially diagnosed by paired samples t-test. This was done separately for participants who were currently taking and those who were not taking vitamin D supplements.

The percentage of participants with abnormal t and z scores was calculated for the whole group of participants who underwent a DXA. BMD (g/cm2) was compared between the results of the DXA carried out previously, before starting the vitamin D supplements, and the results of the DXA carried out in the current study by paired samples t-test. Current BMD measurements (g/cm2) were analysed according to several variables including taking vitamin D supplements, age, gender, BMI, degree of mobility, being on antiepileptic treatment by t-test, ANOVA and Spearman rank correlation test.

Sample size

As the study was based on a previous cohort, the number of eligible subjects was fixed and it was not known at the planning stage how many would actually take part in the study. Additionally, the primary outcome (percentage of participants taking vitamin D supplements) was purely descriptive. The achieved sample size was large enough for univariate analyses but too small for regression analysis.

Results

Participants characteristics

Main characteristics are given in Table 1.

Table 1. Characteristics of the study population

Number of participants	51
Male	29 (56.9%)
Female	22 (43.1%)
Mean [SD] age (years)	51.5 [13.6]
Degree of ID: mild	28 (54.9%)
moderate	15 (29.4%)
severe	6 (11.8%)
profound	2 (3.9%)
Capacitous	18 (35.3%)
Incapacitous	33 (64.7%)
Ethnicity: White	44 (86.3%)
Black	3 (5.9%)
South Asian	2 (3.9%)
Other	2 (3.9%)
Mean [SD] BMI (kg/m^2)	30.2 [7.1]
Mobility: normal	26 (51%)
limited	17 (33%)
wheelchair user	8 (15.7%)
On antiepileptic treatment	23 (45.1%)
Hypogonadism*	5 (9.8%)
History of any fracture	12 (24%)
History of osteoporotic fracture	4 (7.8%)
On vitamin D supplements	41 (80.4%)
Mean [SD] duration of vitamin D treatment (years) in those currently on supplements	7.4 [1.4]

*Figures only include patients with pathological hypogonadism (i.e. do not include women with normal menopause)

Most participants lived in care homes of two to six people with live-in carers or in their own homes, with family or a carer. Five participants lived on their own, albeit in sheltered accommodation and/or with carers visiting regularly. Ten participants were capable of semi-independent living, (e.g. going outside on their own).

Exposure to sunlight was very difficult to quantify. However, it seemed that in the majority of the participants, the time spent outdoors was unlikely to be enough to generate sufficient endogenous vitamin D production. This was also because of very limited skin exposure and the widespread practice of applying high-factor sunscreen before going outside.

Dietary calcium intake varied substantially, mean [SD] 708 [325] mg/daily. However, as many participants were also taking calcium supplements, 90% of the study group either met or exceeded the minimum 700 mg daily calcium intake recommended for adults (British Nutrition Foundation, 2016).

Only 51% of the participants had normal mobility, defined as being able to walk 100 yards unaided (Burke et al, 2017), most of the remaining participants having some mobility impairment and 16% being wheelchair users.

Fifteen women were post-menopausal, one of whom had a history of hypogonadism due to premature menopause from Down's syndrome. Of the seven pre-menopausal women, six had regular periods and one was hypogonadal as she had been amenorrhoeic for over ten years as a result of long-term progesterone treatment and risperidone induced hyperprolactinaemia. Three men had a history of hypogonadism (one from partial hypopituitarism and another two from primary gonadal failure due to Down's syndrome), and two of them had previously been treated with testosterone replacement therapy.

Twentyfour patients were on antiepileptic drugs, ten of whom on monotherapy and fourteen on polypharmacy (thirteen on two antiepileptics and one on three). Carbamazepine was used by twelve patients, valproate by nine, levetiracetam by six, pregabalin by five, lamotrigine by three, phenytoin by two, gabapentin and primidone by one patient each.

Twelve patrticipants (24% of the total study participants) had a history of one or more fractures. In four of these patients (7.8% of the total study participants, three women and one man), these were osteoporotic in nature as evidenced by mechanism and/or site of fracture and/or presence of osteoporosis in a DXA carried out around the same time of the fracture. For 3 of these patients, the fractures had occurred at the age of 44, 54 and 55 years. The fourth patient had experienced a total of six osteoporotic fractures between the ages of 44 and 70 years although in this case a previous history of intermittent oral steroid use could not be excluded. In the other eight participants, fractures were due to significant trauma. One of these eight participants experienced a fracture on two different occasions as a result of self-injurious behaviour.
A total of three patients were or had been on osteoporosis treatment with a bisphosphonate.

Vitamin D
Forty-one participants (80.4%) were still taking vitamin D supplements (mean [SD] duration of treatment 7.4 [1.4] years). These consisted of daily colecalciferol (vitamin D3) in all but two patients (one was taking 50,000 International Units [IU] colecalciferol monthly and the other 50,000 IU ergocalciferol [vitamin D2] monthly). Of the 39 participants taking daily colecalciferol, 4 were on 400 IU/day, 29 on 800 IU/d, and 6 on >800 IU/d (range 1,000 – 3,200 IU/d).

Thirty two participants were taking calcium in addition to their colecalciferol supplements. It was impossible to ascertain precisely the duration of previous vitamin D treatment in the ten participants who were no longer taking supplements, because of uncertainty regarding when the treatment was stopped. However, this ranged between a minimum of one year and a maximum of around three years. The reason for these ten participants not taking vitamin D supplements was a lapse in prescription by the GP rather than lack of adherence by the person.

Mean [SD] serum 25(OH) D levels were 81.3 [21.3] vs 25.2 [10.2] nmol/L ($p<0.0001$) in the participants taking or not taking vitamin D supplements respectively, which were indicative of vitamin D sufficiency and severe vitamin D deficiency respectively (Fig. 1)

Fig.1 Mean (SD) serum 25(OH) D levels in participants taking vitamin D supplements (n=41) and participants not taking vitamin D supplements (n= 10)

In the participants taking vitamin D, the mean 25(OH) D value was 81.3 [21.3] compared with 20.2 [9.4] nmol/L before starting treatment ($p<0.0001$) mean 7.4 years earlier. In participants not taking vitamin D, 25(OH) D levels were not different from when they had been when first measured, 25.2 [10.2] vs 24.1 [6.9] nmol/L.
Total and albumin corrected plasma calcium, phosphate and creatinine levels were normal in all participants.

Bone mineral density
Thirty six participants successfully underwent a DXA scan. Fifteen participants did not, because of: participant refusal (nine cases), exclusion due to lack of potential clinical benefit (four cases, of which two patients on bisphosphonates) or interfering involuntary movement (two cases).
The 36 DXAs carried out in this study and the DXAs previously carried out in the two patients that were on bisphosphonate treatment showed osteoporosis ($t\leq-2.5$) in 23.7% and osteopenia (t= -1.1 to -2.4) in 52.6% of cases. Additionally, of the 25 participants with t scores indicative of osteoporosis or osteopenia, 19 also had z scores of -1.1 or lower, signifying that the majority of patients with abnormal DXAs had decreased bone mineral density not only compared to the normal population at age 30 but also to a reference population of their same age and gender.

The results of the DXAs for the hypogonadal patients were excluded from all subsequent analyses, because of the profound negative effect that hypogonadism per se has on bone. This left a total of 33 participants in whom BMD could be analysed (Table 2).

Table 2. Mean (SD) BMD (g/cm^2) in the participants who underwent a DXA

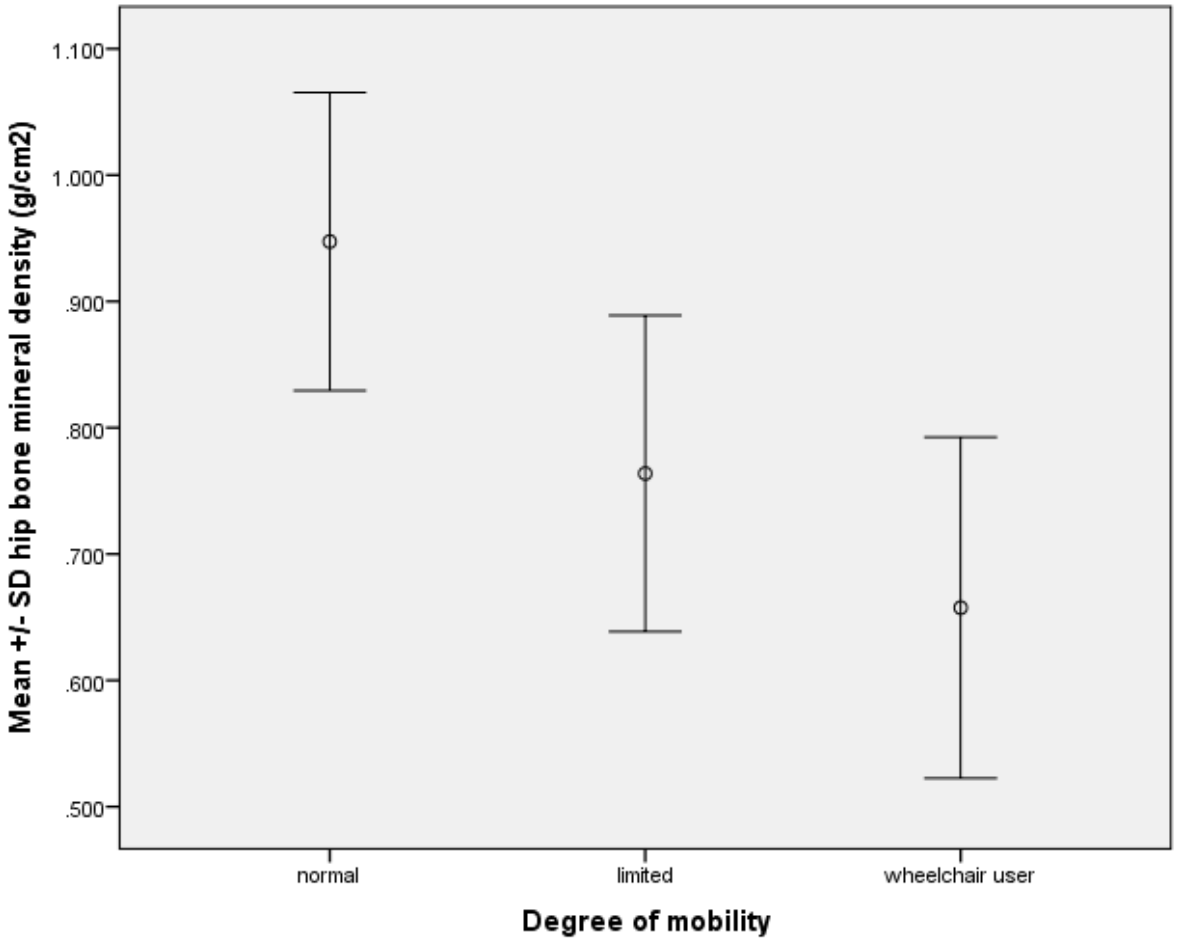
Participants characteristics (n)	Spine	Hip	Femoral neck
Male (20)	0.959 (0.11)	0.854 (0.14)	0.716 (0.13)
Female (13)	0.999 (0.17)	0.774 (0.20)	0.752 (0.23)
On vitamin D (26)	0.980 (0.13)	0.834 (0.18)	0.751 (0.18)
Not on vitamin D (7)	0.947 (0.17)	0.780 (0.11)	0.654 (0.16)
Mild ID (19)	0.980 (0.15)	0.837 (0.18)	0.752 (0.18)
Moderate ID (9)	1.011 (0.99)	0.881 (0.13)	0.780 (0.12)
Severe/profound ID (5)	0.868 (0.12)	0.660 (0.61) *	0.558 (0.17) *
Normal mobility (14)	1.023 (0.12)	0.947 (0.12)	0.798 (0.12)
Limited mobility (13)	0.941 (0.15)	0.764 (0.12)	0.714 (0.20)
Wheelchair user (6)	0.896 (0.11)	0.657 (0.13)#	0.608 (0.19)"
On antiepileptic drug (17)	0.976 (0.16)	0.779 (0.18)	0.699 (0.22)
Not on antiepileptic drug (16)	0.970 (0.11)	0.868 (0.15)	0.764 (0.12)

* p=0.04 vs mild ID
# p<0.0001 vs normal mobility
" p=0.005 vs normal mobility

There was a tendency for a higher BMD (g/cm2) at all sites in participants on vitamin D supplements compared with those who were not (by 3.5% at the spine, 6.5% at the hip and 12.9% at the femoral neck). However, these differences were not statistically significant.

There was a statistically significant difference between participants with normal mobility and those with limited mobility in BMD at the hip (p<0.0001, **Fig. 2**) while the differences at the spine and at the femoral neck were of borderline statistical significance (p= 0.05 and 0.057 respectively). However, the magnitude of the difference was substantial, particularly in wheelchair users. In these patients, mean BMD values were lower by 12.4% (p= 0.054), 33.0% (p<0.0001) and 26.9 % (p= 0.005) at the spine, hip and femoral neck respectively compared to participants with normal mobility.

Fig. 2 Mean (SD) BMD at the hip according to degree of mobility



There was no correlation between BMD measured at any site and age or total daily calcium intake and no difference in BMD according to gender, ethnicity or being on antiepileptic treatment. There was a highly significant correlation between BMI and BMD measured at all sites (p= 0.01). Participants with a history of fracture had a non significant trend to a lower BMD at the spine (p= 0.065) and the femoral neck (p= 0.089), by 10.2% and 14.9% respectively.

Because of the large differences in BMD according to degree of mobility, particularly in wheelchair users, all the analyses were repeated after the exclusion of these patients. This left a total of 26 participants in whom BMD could be analysed (Table 3). In this case, those on vitamin D supplements had a significantly higher BMD at the hip (by 16.3%, p= 0.031) and at the femoral neck (by 24.3%, p= 0.016) while a 5.9% higher BMD at the spine was not statistically significant.

Table 3. Mean BMD in participants taking or not taking vitamin D supplements (patients with hypogonadism and wheelchair users excluded)

Mean (SD)BMD (g/cm^2)	Patients on vitamin D (n=7)	Patients not on vitamin D (n=19)	*P*
Spine	1.003 (0.125)	0.947 (0.17)	0.393
Hip	0.907 (0.131)	0.780 (0.108)	0.031
Femoral neck	0.813 (0.131)	0.654 (0.161)	0.016

There was no association between BMD measured at any site and age, ethnicity, total daily calcium intake, and antiepileptic treatment. There was a tendency for men to have a lower BMD than women, with a significant difference at the femoral neck (p=0.004). There was a highly significant correlation between BMI and BMD measured at all sites (p= 0.01). People with a history of fracture had a significantly lower BMD at the femoral neck (p= 0.046) and a non significant trend to a lower BMD at the spine (p= 0.09), by 17.7% and 10.7% respectively.

Evidence for long term effects of vitamin D

Seventeen of the 32 participants with a current DXA scan, had also had a DXA when initially diagnosed with vitamin D deficiency. Of these 17 patients, 16 had taken vitamin D supplements continuously for an average of 7.4 years and were still taking them. The remaining patient had only taken vitamin D supplements for approximately a year and had stopped them several years before the current study, hence it was necessary to exclude him from this analysis. In longitudinal analysis in the 16 patients still taking vitamin D, a 6.1% increase in BMD was seen at the spine (p=0.004) while no change was seen at the hip. After the exclusion of the wheelchair users, 9 ambulant patients had taken vitamin D supplements continuously for an average of 7.4 years and were still taking them; their BMD increased by 6.6% at the spine (p=0.032) while no significant change was seen at the hip.

No paticipants developed any biochemical or clinical suggestion of vitamin D toxicity (i.e. hypercalcaemia, 25(OH)D levels >150 nmol/L or nephrolithiasis) while on vitamin D supplementation.

Discussion

Our study shows that the majority of people with intellectual disabilities had no difficulties in remaining on vitamin D supplements in the long-term. Additionally, people who were on treatment had sufficient serum 25(OH)D levels while those not on Vitamin D supplements had mean 25(OH)D levels indicative of severe vitamin D deficiency. Vitamin D treatment for an average of seven years with adequate serum levels of 25(OH) D was associated with a 6% increase in bone mineral density at the spine and no deterioration in BMD at the hip.

The BMD increase at the spine is consistent with improvements seen in other studies in patients treated for vitamin D deficiency and compliant with vitamin D supplementation (Adams et al, 1999; Kantorovich et al, 2000; Ferlin et al, 2015; Geller et al, 2008).

Moreover, given the downward trend in BMD seen in the general population from the fifth decade of life (Compston, 1990) the stabilisation of hip BMD observed in our study participants treated with vitamin D between mean age 44 and 51 years can also be considered a clinically useful result.

In the group as a whole, a tendency towards a higher BMD in people who were currently on vitamin D supplements compared to people who were no longer taking them was found at all anatomical sites examined but the differences were not statistically significant. However, large and statistically significant differences were observed when participants with major confounders, namely hypogonadism and lack of mobility, were excluded from the analyses.

Investigation of other factors that could influence BMD

We found no association between BMD and age or gender. This is at odds with findings in the general population, in which bone mineral density declines with age, particularly in postmenopausal women (Compston, 1990). Additionally, BMD was similar between

participants on antiepileptic treatment and those who were not. However, the negative effects of antiepileptic agents on bone have been partly explained by increased serum vitamin D catabolism and relative vitamin D deficiency (Hollo' et al, 2014). As the majority of our study participants had adequate serum vitamin D levels, this may have counteracted any negative effects of antiepileptics mediated by vitamin D deficiency.

We also found no association between BMD and total daily calcium intake. However, for 90% of the participants who underwent DXA this was 700 mg or more, which is in line with current guidelines (National Institute for Health and Care Excellence, 2016; National Osteoporosis Society, 2013), and was achieved by diet alone or, in most cases, with the addition of supplements.

Limitations in mobility were associated with a graded, marked decrease in BMD, particularly at the hip. This finding is highly relevant, given the frequency of physical or behavioural obstacles to mobility in people with ID. It is also similar in the general population, where the duration of sedentary behaviour is negatively associated with BMD at the hip but not at the spine (Chastin et al, 2014). Lack of weight bearing exercise has long been proven to induce bone loss (Mianire et al, 1975; Zerwekh et al, 1998) and impaired mobility has been associated with low BMD in previous studies specifically in people with ID (Jaffe et al, 2005; Lohiya et al, 2004). Methods to improve mobility in a safe way could be investigated and implemented through ID people and carers education and the involvement of physiotherapists. For people with the most severe physical impairments, the use of mechanical aids (such as standing frames, slings or standing wheelchairs) to facilitate an upright, weight bearing posture should be considered. Additionally, the use of sclerostin inhibitors may hold some future promise for these patients, whenever any such drugs will be licensed (Spatz et al, 2013).

Although the percentage of hypogonadal individuals in our group was very high (9.8%) and in line with other studies (Srikanth et al, 2011; Hawli et al, 2009; Center et al, 1998), the absolute number (five participants, of whom only four had a DXA) was too small to allow statistical analysis. Hypogonadism should be viewed as a common problem in people with ID. It has been established by a large body of literature that hypogonadism leads to osteoporosis and increased fracture risk, in both women and men. Hence, its presence should be actively investigated in the ID population and fracture prevention strategies considered. This is particularly true for people with Down's syndrome, in whom hypogonadism is highly prevalent, and for women on longterm progestin induced amenorrhoea. These are two subgroups in which osteoporosis and fracture risks are very high (Hawli et al, 2009; Geijer et al, 2014; Arvio et al, 2009). Whether patients with long-term antipsychotic induced hyperprolactinaemic hypogonadism have an increased fracture rate has not been determined although there is a suggestion that these patients have reduced bone mineral density (Frighi et al, 2011). Moreover, it has long been established that all patients with untreated hypogonadism, irrespective of its cause, have a high fracture risk (Reifenstein and Albright, 1947).

BMI was positively and significantly associated with BMD so that individuals with lower BMI were also those with lower BMD. This is in keeping with findings in the general population although the contribution of BMI to fracture risk in the general population is not linear and is seen mostly at BMI levels below 25 (De Laet et al, 2005).

Prevalence of osteoporosis and osteopenia

In our cohort, the prevalence of osteoporosis and osteopenia (24% and 53% respectively) was broadly similar to findings in previous studies in people with ID (Srikanth et al, 2011; Jaffe et al, 2005; Lohiya et al, 2004; Geijer et al, 2014; Lin et al, 2014). Comparison with the most recent and largest study in the general population (Wright et al, 2014) shows that the prevalence of osteoporosis and osteopenia in our study participants is respectively about four and two times as high as that of people of approximately similar age. In fact, the prevalence of osteoporosis in our study participants, at a mean age of 51 years, was actually higher than in individuals aged 70-79 years from the general population. For osteopenia, the prevalence in our study participants was higher than in those aged 80 years and over (Wright et al, 2014). The marked excess in osteoporosis and osteopenia in women, consistently seen in the general population, was not observed in our study participants.

History of fractures

Fracture is the most important potential adverse outcome of poor bone health and is particularly difficult to manage in the ID population.

Four of our study patients had a history of one or more osteoporotic fractures, the first fracture occurring in middle age. This is very different from the general population, in whom the mean age at first osteoporotic fracture is approximately 70 years (Abrahamsen et al, 2015). Additionally, one participant had two consecutive fractures as a result of self- injurious behaviour, which emphasizes the importance of prevention of such behaviour.

Limitations of the study

The main limitation of our study is the small number of participants. Recruitment of people with ID into clinical research including physical and radiological measurements, together with blood sampling, poses multiple difficulties and is rarely attempted on a large scale. Hence studies on the scale reported here can provide evidence base for practice. However, while observational studies including more participants could be envisaged, the established clinical need for treatment of vitamin D deficiency makes it impossible to carry out a randomised controlled trial of vitamin D. Additionally, given that all but one of the participants still on vitamin D who underwent a DXA were also taking calcium supplements, it is not possible from this study to infer whether any benefits achieved from vitamin D supplementation would be achieved also without concomitant calcium supplementation.

Interpretation of findings and conclusions

Our study suggests that long-term vitamin D treatment improves or at least stabilises bone mineral density in people with adequate calcium intake (which, in our group, was mostly from supplements). Additionally, it may counteract some of the negative impact that antiepileptic therapies, commonly used in the ID population, have on bone. However, approximately a quarter of ID people have osteoporosis irrespective of vitamin D treatment, which may already put them at risk of fractures in middle age. This should lead to two conclusions. The first is that diagnosing vitamin D deficiency in people with ID at a mean age of 44 years, as we did, might be too late to have a more significant impact. Secondly, other risk factors for osteoporosis and fractures should be actively investigated in the ID population. Our current study points to impaired mobility and hypogonadism as two such risks given their high prevalence in ID individuals and their hugely negative impact on bone health.

Future directions

The high risk of osteoporosis and fractures in ID people should be better recognised as a clinical and public health problem. A large, adequately powered study on the risk factors for fractures in these individuals would properly establish the optimal targets for intervention. Meanwhile, given the wide prevalence of vitamin D deficiency and the acceptability, safety and efficacy of vitamin D supplements, screening for and treatment of vitamin D deficiency should be offered to people with intellectual disabilities from an early age, ensuring that calcium intake is adequate.

Conflict of interest statement

VF holds a grant from the National Institute of Health Research (NIHR) for a study on fractures in patients with intellectual disabilities. GMG is a NIHR Senior Investigator. The views expressed in this publication are those of the authors and not necessarily those of the NIHR, the National Health Service or the Department of Health.

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