Review article

A critical review of exercise training effects on bone mineral density (BMD) in early postmenopausal women

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Abstract
Objectives: To review evidence of positive exercise effects on BMD in early postmenopausal women (0.5–8 years postmenopausal) by summarising existing studies in this area.

Data sources: MEDLINE search using the terms “exercise” AND “BMD” AND “osteoporosis”, later than 1970, plus the bibliographies of the studies identified by the MEDLINE search.

Study selection: Nine studies were identified and included in this review. All the studies included a non-training control group, half of them were randomised.

Data extraction: Exercise effects on bone mineral density at the hip and the spine were qualitatively compared predominantly based on the type of exercise and study duration. A quantitative analysis was not possible due to the inhomogeneity of the studies.

Data synthesis: 5 out of 7 studies (6 out of 9 exercising subgroups) demonstrated significant positive exercise effects defined as BMD differences in the exercise versus control group at the lumbar spine, and 3 out of 6 at the proximal femur. Intervention periods of all studies showing no positive results were shorter than nine months. However, only 3 studies showed significant positive BMD changes in the exercise group alone. All of these studies used mixed exercise regimes using high impact exercises and resistance training.

Conclusion: The results suggest that in particular exercise programmes with high impact and resistance training lasting longer than a year help to maintain or even improve BMD at the lumbar spine and hip in early postmenopausal women. Keywords: osteoporosis, BMD, exercise, training, early postmenopause

Dr Wolfgang Kemmler, PhD

Wolfgang Kemmler was born in 1964 in Tübingen, Germany. After 4 years of military service he studied sport economics at the University of Bayreuth with a focus on medicine, health, and fitness. His diploma thesis was entitled “Diagnostic possibilities to determine overtraining”. After a postgraduate period in Amsterdam he started his Ph.D. studies with his doctorate at the Institute of Sports Medicine, University of Bayreuth in 1993 and finished in 1996 with a thesis entitled “Exercise and osteoporosis”. In 1997 he joined the Osteoporosis Research Center at the Institute of Medical Physics, University of Erlangen-Nürnberg. His research is focused on exercise effects in bone, bone muscle interactions and exercise benefits during menopause as well as periodisation schemes of strength training. In 2003 he finished his habilitation thesis “Exercise in the early-postmenopause” using results from the Erlangen Fitness Osteoporosis Prevention Study (EFOPS).
Introduction
The effect of the oestrogen decline during the early postmenopausal years is complex. As oestrogen receptors are abundant throughout the body many organ systems are affected. One consequence of oestrogen depletion is accelerated bone loss. Hormone replacement therapy (HRT), which is still widely used as a major prevention strategy, has recently become a controversial treatment, in particular, because of negative cardiovascular effects.

Thus different preventive approaches are gaining wider attention. One option is adequate physical activity or exercise. There is some evidence that during the early menopausal years exercise may compensate at least some of the negative effects caused by hormone depletion. In healthy men and premenopausal women positive exercise effects on bone mineral density (BMD) were demonstrated in numerous studies. However, in early postmenopausal women results are ambivalent. When for example comparing given exercise programmes in pre- and (early) postmenopausal women positive effects were observed in the pre- but not in the early postmenopausal cohort.

This effect can possibly be explained by using the set point theory according to which oestrogen (E) or oestrogen receptors (ER) modulate the adaptive response of bone to mechanical strain. Therefore mechanical strains may trigger a response of bone under premenopausal hormonal conditions but may no longer do so once the adaptive threshold has increased with hormone depletion. As a consequence exercise may have to be adapted to the targeted population but it is difficult to summarise recommendations from the current literature, in particular as a wide variety of exercise regimen has been used.

This article reviews the current literature with respect to the following questions: what are the general effects of “exercise” in early postmenopausal women and which particular exercise regimes do positively affect BMD. Further, the authors want to increase the reader’s awareness of methodological problems that may severely limit the interpretation of exercise studies.

Methods
Identification of eligible studies
A MEDLINE search was conducted using the terms “exercise” AND (“BMD” OR bone mineral density) AND “osteoporosis” in the title, key words and abstract between 1970 until 2003. There were no limits with respect to age, gender, or type of publication. From the results the interventional studies were filtered out. The bibliographies of thee publications were also screened for articles not found in MEDLINE. For this review, all studies that investigated early postmenopausal cohorts or subgroups were used. Early menopause was defined in agreement with the literature as 0.5-8 years after the last menstrual bleeding. Publications that did not include the time range since menopause, or did not focus on BMD, were excluded. Further, studies that did not include a non-training control group or did not report the results of the control group separately were also excluded.

Results
The table (Table 1) shows details of the nine studies identified. Five of them were randomised and four non-randomised trails. The size of the exercise groups

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**Dr Klaus Engelke, PhD**

Klaus Engelke was born in Hannover, Germany and studied physics at the University of Hamburg, Germany. During his Ph.D. studies at the Hamburger Synchrotron Radiation Lab (Hasylab) at the German Elektronen-Synchrotron (DESY) he pioneered µCT and finished his Ph.D. thesis “µCT with synchrotron radiation to quantitatively determine bone mineral” in 1989. During a short post-doc period at the university hospital in Hamburg where he developed applications for µCT he joined the Osteoporosis Research Group (ORG) at the University of California at San Francisco (UCSF) in 1991 to work on quantitative analysis of bone structure and density as well as on quality assurance and study design of pharmaceutical trials in osteoporosis. Since 1995 he has been head of the Osteoporosis Research Center at the Institute of Medical Physics, University of Erlangen-Nürnberg where he continued his research in osteoporosis focusing on methodological aspects. Other research fields are advanced image processing and the design and application of µCT apparatus.

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varied from 5 to 50 subjects. In terms of the WHO criterion osteopenic subjects were included exclusively in one of the studies and predominantly in the study by Sugiyama et al. Attendance rates varied from 50% to 90%. Two studies exclusively employed aerobic or jumping exercises, three studies on resistance training, and four studies used mixed training protocols with aerobic, resistance, and jumping exercises.

Intervention periods varied from six to 24 months. Calcium was supplemented in three studies to ensure a total calcium intake of ≥1500 mg/d. Eight studies employed dual photon (DPA) or dual xray absorptiometry (DXA) to measure BMD at the lumbar spine (LS) (n = 8) and/or the proximal femur (n = 6). Two studies additionally used quantitative computed tomography (QCT) at the lumbar spine or the proximal femur.

BMD results measured by DXA or DPA are summarised in Figure 1 for the lumbar spine and in Figure 2 for the hip. In the spine the BMD changes are in particular heterogeneous in the exercise groups ranging from −2.0% in six months to +2.5% in nine months. In the control group (CG) there was always a loss but the difference among the studies was even larger than among the exercise groups. If the net exercise effect is defined as the difference between EG and CG, two studies showed no exercise effect while five studies (i.e. seven out of nine exercise subgroups) demonstrated at least a positive net effect after exercise intervention. In six out of nine subgroups this effect was significant (p<0.05). One study that used QCT showed a +7.0% (p<0.001) difference for trabecular and a +4.8% difference (p<0.001) for cortical BMD of the lumbar spine.

Figure 1: BMD changes at the lumbar spine. #: randomised studies

![BMD Lumbar Spine (DXA)](image-url)
Exercise in postmenopausal women

As expected in the proximal femur overall changes were smaller. Fewer studies showed significant differences between exercise and control groups but it should be pointed out that Figure 2 shows results for three different regions, the total hip, the neck, and the trochanter, thus care must be taken when comparing study results at the proximal femur. In the total hip region net exercise effects varied from +0.4% to +1.4%, in the neck from −1.9% to +1.9%, and for the trochanter the only study reported a net effect of +2.3%. Using QCT at the proximal femur a 3% difference (n.s.) was found after 12 months.

Discussion

A coherent interpretation of exercise effects in early postmenopausal women is difficult due to three major and several minor reasons. The major reasons are: (1) the number of existing studies is small and their design is very heterogeneous. (2) As it can be seen from Table 1 the exercise regimens vary largely, (3) the number of study subjects per group is most often small (<20) and the intervention periods rarely extend beyond 12 months.

Using the definition of early menopause as 0.5-8 years after the last menstrual bleeding, the authors identified nine interventional studies. As is well known, the most relevant reductions in bone density occur around the menopause, a narrower window of 0.5-3 years may be more appropriate, but for this period there is only one study; the other eight studies include women of a significantly broader postmenopausal age range. A comparison of studies including subjects of different menopausal age ranges is difficult. An additional problem in Heikkinen’s study is that only BMD data of the trochanter is included, but no data is provided for the spine or the total femur.
Apart from menopausal age the bone status at the start of a study may play a major role in the outcome. This has been demonstrated in a study comparing exercise effects on BMD in healthy, osteopenic, and osteoporotic women. Significant differences were found at the femoral neck for the osteopenic and osteoporotic groups (+1.3%) when compared to the healthy group (-1.0%). At the spine there were no differences between the groups. These results should be kept in mind when trying to summarise the results of exercise. From Table 1 it can be seen that one study exclusively recruited osteopenic women. A second study recruited predominantly osteopenic women. Furthermore, an inadequate calcium and Vitamin D intake can impact on the results, in particular if osteopenic or osteoporotic women are investigated. From the nine studies included in this review, Ca was supplemented in only three and Vitamin D in two studies.

A general problem in the comparison of exercise studies is the great variation of exercise regimen. In addition the description of the exercise regimen is often incomplete. This applies to all age ranges, not only to early postmenopausal women. For example, effects of swimming, jumping, and running on bone are very different. In the nine studies listed in the table exercise regimen included fast walking, running, low and high impact aerobic, jumping, and isometric and/or dynamic resistance training in various combinations. In addition the exercise quantity, typically described in terms of strain rate, strain magnitude, strain-frequency, and cycle-number varied greatly among the studies. Despite this large variety five out of seven studies demonstrated significant positive net effects on BMD at the lumbar spine and three out of six at the hip. The variety of exercise regimen is more evident when looking at the BMD loss or gain of the exercise and control groups separately.

It must be emphasised that the intervention periods were different. Obviously one cannot simply scale the results in Figures 1 and 2 linearly to 6 months, the shortest period used. But in those studies with longer follow-up times exercise effects increase over time, at least during the first 12 months. This can be easily understood as the cancellous activation-resorption-formation remodelling sequence of bone takes approximately 200 days. Thus apart from the three older studies the net exercise effects of the remaining exercise studies are comparable. The three older studies also used DPA, a predecessor of DXA, to measure BMD, and the number of subjects per sub-group was always less than 20. Further, the decrease in the control groups assessed in these three studies was much larger than the average of 1-2% at the spine and 1-1.5% at the hip reported for women during in early menopause. The BMD loss in the control groups in the other 5 studies is more in line with the expectations for normal or osteopenic women of that postmenopausal age.

Drawing conclusions about the most favourable type of exercise optimising effects on BMD from the nine studies is a daunting task, even if the three older studies are not considered. Depending on exercise intensity, rate, and volume, all exercise types employed are potentially bone anabolic. Resistance training with high strain magnitude is known to affect bone, despite the fact that Bemben et al. could neither demonstrate positive effects at the LS in their high- nor in their low-intensity exercise groups. Probably the intervention period was too short; also the sub-groups were extremely small.

Jumping exercises, which produce high strain magnitudes and rates, increase bone strength at the lower limbs and the lumbar spine in rodents. In premenopausal women, jumping exercises also showed positive effects on BMD of the hip and the lumbar spine. However, in Bassey’s and Sugiyama’s studies identical exercise regimen failed to demonstrate the same effects in (early) postmenopausal women. This is in contrast to animal studies. For example, with jumping exercises the same effects in osteopenic ovariectomised and Sham-operated rats were obtained.

The osteoanabolic relevance of walking is still under discussion. There are some reports that brisk walking affects lumbar spine BMD in osteopenic women but there is even more evidence that in healthy women with normal physical activity ground reaction forces induced by walking (1-1.5 x body weight with low strain rates) are too low to increase BMD. These data are also supported by the results of Martin et al., which observed a 1.7% reduction of LS-BMD after walking at 70-85% HFmax.

All those studies listed in the table that used mixed exercise regimens with high impact
exercises (3-5 x body weight) and resistance training \(^{21,22,25,26}\) demonstrated positive effects on BMD of the lumbar spine and the hip. We think that this is the most favourable regimen and we also used it in our studies. However, it must be stated that, based on the nine studies analysed in this review, this thesis cannot be fully proven, although it is obviously supported by the data. Criticism has been raised that high impact exercises \(^5\) and prolonged heavy loading \(^9\) may unfavorably affect osteoarthritis and low back pain. Contrarily, in our ongoing five year exercise study from which we only used the published two year data for this review \(^{26,55}\) even after four years a significant pain reduction at the spine and no change at the joints was observed. The authors attribute this fact to their exercise design, with a prolonged phasing in period during the first seven study months, and regenerational periods following each heavy loading period. Thus their results suggest that bone maintenance and pain reduction are not conflicting endpoints as claimed by Turner \(^56\).

As can be seen from Table 1 and Figures 1 and 2, there is no evident difference between the five randomised and the four studies not randomised. While the double blind randomised design is mandatory in pharmaceutical trials there is some ambiguity in exercise studies because these cannot be blinded. There are conflicting data on the bias introduced by different motivation levels in non-randomised controlled exercise studies. Wolff et al. \(^11\) concluded in their meta-analysis that non-randomised controlled studies showed an exercise effect twice as high compared to randomised studies while the meta-analysis published by Kelley \(^8\) showed the opposite effect (effect size: 1.08 vs. 0.44).

One point of critique should be mentioned here with respect to randomised exercise trials. It is most often not clear whether authors included subjects that refuse to take part in the study after randomisation but before the actual start of the exercise sessions in their reported dropout rates. The subjects may not like the group they have been randomised to and quit right away. To which degree this effect offsets randomisation has to the authors’ knowledge not been investigated yet. Thus all exercise studies should report dropout rates between recruitment and actual start of the exercise program and separately dropout, attendance and compliance rates during the intervention period. Also, exercise and physical activity levels outside the study intervention in particular in the control group must be carefully monitored.

There are several other confounding factors that may clutter exercise effects on bone and that are often not carefully monitored. This makes it extremely difficult to interpret exercise studies. Important confounding factors are:

- Diseases or medication affecting bone metabolism. Most studies exclude subjects at baseline but often they do not control these factors during the study.
- Weight changes affect bone mineral density and should be carefully monitored.
- Nutritional changes, in particular diets or changes in the Ca and Vitamin-D intake may also impact on bone mineral density.

**Conclusion**

So far nine studies analysed exercise effects with respect to bone (BMD) in early postmenopausal women. Due to the inhomogeneities in their design, exercise regimen and results presented it is very difficult to compare them and to extract exercise recommendations. Overall, regimes with high impact and resistance exercises were most favourable. There is a need for studies with longer follow up times (> 12 months) and larger well defined populations that are carefully monitored for confounding factors.

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References


24. Martin D, Notelevitz M. Effects of aerobic training on bone mineral


### Table 1: Characteristics of exercise studies for the prevention of bone loss in early-postmenopausal women

<table>
<thead>
<tr>
<th>Author</th>
<th>YsM</th>
<th>Number with data</th>
<th>Rmised</th>
<th>Diseases, medication affecting bone at baseline</th>
<th>Longitudinal control of variables affecting bone</th>
<th>Calcium intake baseline</th>
<th>Calcium supplementation</th>
<th>Exercise intervention</th>
<th>Exercise description</th>
<th>Compliance, Drop-out, Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bemben 2000</td>
<td>1-7 y (41-60)</td>
<td>EG: 10/7 CG: 8</td>
<td>yes no</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Cheng 2002</td>
<td>0.5-5 y (50-55)</td>
<td>EG: 12 CG: 15</td>
<td>yes no</td>
<td>yes no medication diseases?</td>
<td>no</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grove 1992</td>
<td>1-8 y (49-64)</td>
<td>EG: 5/5 CG: 5</td>
<td>yes no</td>
<td>yes no diseases, no exclusion of HRT</td>
<td>no</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heikkinen 1997</td>
<td>0.5-3 y (49-55)</td>
<td>EG: 13 CG: 12</td>
<td>yes no</td>
<td>yes no</td>
<td>no</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kemmler 1998</td>
<td>1-8 y (47-59)</td>
<td>EG: 15 CG: 18</td>
<td>no no</td>
<td>yes</td>
<td>no</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kemmler 2003</td>
<td>1-8 y (48-61)</td>
<td>EG: 50 CG: 33</td>
<td>no no</td>
<td>yes</td>
<td>no</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

- Calcium intake baseline: 900 mg/d (EG 1), 1570 mg/d (CG)
- Calcium supplementation: up to 1500 mg/d
- Exercise: Warm-up, resistance training (all major muscle groups)
- 3’60 min/w, 8 exercises 3 sets (EG 1) 8 reps. with 80% 1RM vs. (EG 2) 16 reps. with 40% 1RM; 6 months
- Attendance: ≈90%, Drop-out: 29% (EG)
- High impact exercises, resistance training (3-4 exercises for the upper trunk)
- 6”(2) joint sessions/w =200 jumps/session. (GRF: 3-5times body weight), description resistance training?; 12 months
- Attendance? joint session ≈50%, Drop-out: 40% (EG)
- Warm-up, aerobic training (weight bearing), resistance exercises (non-weight-bearing)
- 3’60 min/w, 20 min of aerobic training: (low (LI) vs. high impact (HI)); 12 months
- Attendance: ≈81%, Drop-out: 10% (EG)
- Resistance training (aerobic, isometric and dynamic resistance exercises)
- 2’60 min/w; 20 min aerobics at 70% Hfmax, 12-15 isometric exercises 2-3 sets; 3-4 dynamic exercises, 2-4 sets 10-15 reps; 9 months
- Compliance?, Drop-out: 4% (EG + CG) Poor exercise description
- Endurance exercises, low and high impact aerobic, multi-directional jumps, dynamic and isometric resistance exercises
- 4’/w., 20 min aerobics at 70% Hfmax, 12-15 isometric exercises 2-3 sets; 3-4 dynamic exercises, 2-4 sets 10-15 reps; 9 months
- Compliance: ≈70%, Drop-out: ≈5% (EG)
- CG not exclusively early postmenopausal
- Endurance exercises, low and high impact aerobic, multi-directional jumps, dynamic and isometric resistance exercises
- 4’/w., 20 min aerobics at 70% Hfmax, 80 jumps (GRF: 3-5 times body weight), 10-13 resistance exercises, 2-4 sets 3-10 reps at 70-90% 1RM 24 months
- Compliance: ≈70%, Drop-out: 18% (EG)
<table>
<thead>
<tr>
<th>Study</th>
<th>Duration (y)</th>
<th>Age (M±SE)</th>
<th>EG</th>
<th>CG</th>
<th>Calcium Suppl.</th>
<th>Exercise</th>
<th>Attendance</th>
<th>Drop-out</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martin 1993</td>
<td>1-6</td>
<td>20/16</td>
<td>yes</td>
<td>no</td>
<td>1000 mg/d</td>
<td>Aerobic training (fast walking on treadmill)</td>
<td>81%</td>
<td>31%</td>
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<tr>
<td>Pruitt 1992</td>
<td>1.7</td>
<td>55±1</td>
<td>no</td>
<td>no</td>
<td>812 mg/d (EG)</td>
<td>Warm-up, resistance training (all major muscle groups)</td>
<td>83%</td>
<td>0%</td>
</tr>
<tr>
<td>Sugiyama 2002</td>
<td>2-5</td>
<td>48-55</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>Vertical jumping exercises</td>
<td>82%</td>
<td>?</td>
</tr>
</tbody>
</table>

Key: YsM: years since menopause; Rm-ised= randomised; EG: exercise group; CG: control group; w: week; d: days, min/w: minutes; Hf\textsubscript{max}: maximum heart frequency; reps: repetitions; 1 RM: 1 repetition maximum; Ca: Calcium; suppl.: supplementation