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Perspective Article

What is the prescription for healthy bones?

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Defining an optimal exercise prescription for promoting bone gain, reducing bone loss and ultimately preventing osteoporosis-related fractures has been the focus of much work over the past 20 years. While we can easily prescribe exercise for improving cardiovascular and muscle health, there is currently no clear prescription for improving bone health. Millions of women and, more recently men, are searching for alternatives to drugs to prevent fractures related to low bone mass. In order to easily prescribe an exercise regimen for improving bone health, we must make the regimen simple for health practitioners to prescribe and thus, our approach in developing a prescription needs to be more similar to that of clinically testing a drug – systematic, quantitative and well controlled in human models.

Osteoporosis has reached crisis proportions. Approximately 7.8 million women and 2.3 million men in the U.S. have osteoporosis[1]. Another 21.8 million women and 11.8 million men have low bone mass. These numbers are expected to double in the next 50 years. While there is frenetic research to develop pharmaceutical prescriptions, there is a growing public need to promote a healthy lifestyle. Exercise prescription is a central part of that demand.

An exercise prescription defines the mode, intensity, frequency and duration of exercise required to stimulate osteogenesis. An exercise prescription must also consider the following principles of training: specificity, overload, reversibility, initial values and diminishing returns[2]. Using the cardiovascular model for exercise prescription the bone-exercise field has learned that the skeletal system is unique compared to the cardiovascular and muscular systems in several ways:

Response time is very slow. Due to the long remodeling cycles for bone of 3-6 months, interventions must last a minimum of 6 months, but are best at 1-2 years and longer.

Changes are small. A 2% increase in bone mass can translate to large reductions in fracture risk[3]. These small changes are in contrast to the large changes often observed in cardiovascular and muscle systems.

Bone has a "lazy zone"[4]. The lazy zone describes a lack of sensitivity and subsequently a lack of response in bone to a stimulus that would elicit a change in the cardiovascular or muscular systems. This is why, for example "jogging" programs haven't demonstrated measurable changes in hip bone mass – jogging is too similar to normal daily activity[5,6].

Bone appears to remember childhood patterns of activity[7-9]. The skeleton is unique in that participation in physical activity during childhood is related to adult bone mass. Thus, building bone during youth is identified as a primary strategy to prevent osteoporosis later in life.

Bone has a different metric for intensity. The metric for the cardiovascular system is a percentage of maximum heart rate or maximum VO2. The metric for intensity for muscle is a percentage of 1 repetition maximum (1 RM) or 6-8 RM. The metric for intensity for bone in humans has yet to be defined. However, intensity for bone in the animal model has been identified as a function of strain rate or how fast bone is deformed[10]. Strain rate is a function of the magnitude of bone deformation (strain) and the frequency of loading. However, strain is measured directly on the bone in animals, an unethical method to use in humans. Therefore, a metric based on externally measured variables that cause bone to deform such as ground reaction forces (GRFs), estimated joint reaction forces (JRFs) and their respective rates of application has been proposed and must be quantified[11].

Older bone is less responsive to loading than is younger bone. After 9 months we noted no changes in BMD in postmenopausal women participating in a weighted vest plus impact exercise[12]. However, after 5 years, we observed that those who continued the program maintained hip BMD at all regions while controls lost bone. The most dramatic increases in BMD were in those not on estrogen. In fact, two women reversed their osteoporosis. By contrast, in a similar progressive program of weighted vest plus impact exercise, mature premenopausal women (30-45 yrs) gained 2.5% hip BMD after 12 months[13]. Similar findings have been reported by Bassey et al., who showed that pre- but not postmenopausal women gained hip BMD after similar jumping interventions[14].

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Reversibility applies to adults and not growing bone. In a progressive program of weighted vest plus impact exercise, mature premenopausal women (30-45 yrs) gained 2.5% hip BMD after 12 months[13]. However, significant bone loss was observed after just 6 months of detraining. We have observed similar effects in gymnasts who lose bone during 3 months of off-season detraining and gain bone during 9 months of training[15]. Thus, in the adult skeleton, detraining is associated with bone loss. In contrast, Fuchs et al. found that gains in hip bone mass from participating in 7 months of drop landings were maintained in prepubertal children after 7 months of detraining[8].

While the research to date has generated more focused exercise recommendations, we are still lacking the more precise exercise prescriptions that exist for both the cardiovascular and muscular systems. To most effectively develop a prescription for bone health, a dose-response design is required as is done for prescription drugs and as has been done for improving aerobic capacity. Most drug trials apply the parallel dose design to assess optimal dosing prior to FDA approval. This approach has been used widely in animal studies of bone and exercise[16-22]. For example, the work of Cullen et al. provides us with a model for studying the dose response of bone to exercise and thus a scientific basis on which to build an exercise prescription[16]. Adult rat tibiae were loaded in four-point bending at 25 or 30 N for 0, 40, 120, or 400 cycles at 2 Hz for 3 weeks. As the strain magnitude decreased, the number of cycles required for activation of formation increased. Thus, the authors concluded that at constant frequency, the number of cycles required to activate formation is dependent on strain and that, as the number of cycles increases, the bone response increases. Controlled dosing such as this provides the necessary data to develop an effective exercise prescription for bone. However, this controlled dosing proves to be difficult in humans.

A majority of human-based research in bone and exercise has used broad programs of multiple resistance training exercises and cardiovascular regimens to increase bone mass[24-31]. While several of these studies attempt to manipulate only one variable, there are in fact several dose-related variables manipulated. For example, Kerr et al. had two cohorts perform the same resistance training exercises, but at different intensities based on muscle strength[29]. A strength group performed 3 sets of 8 RM and an endurance group performed 3 sets of 20 RM. While the load magnitude of each exercise was different between groups, so were the repetitions and quite probably the loading rate. Therefore, three variables potentially related to osteogenesis (load magnitude, loading rate, and repetitions) were manipulated. While performing a combination of twelve resistance exercises at 3 sets of 8 RM caused an increase in hip BMD in postmenopausal women, it is not known whether the change was due to the difference in load magnitude, loading rate or repetitions. Before we can prescribe individualized exercise programs for bone health, we need to develop a response surface based on only one mode of exercise.

To generate points on the dose-response surface for human bone, researchers must define the primary outcome variable and the dose. The primary outcome variable should be located at a clinically relevant fracture site (i.e., hip and spine) and should be easily measurable (i.e., BMD and geometric properties). The dose variable must include the standard components of an exercise prescription, paying careful attention to use an intensity metric most likely associated with bone strain[11]. In addition, the length of dose application, and magnitude of dose required to maintain exercise-induced bone gains must be considered as well. Recent evidence from the Bone Research Group of the UKK in Finland indicates that bone gains from tennis playing are maintained even when hours of playing time are reduced by more than half[23]. Therefore, while loading rate and load magnitude were assumed the same, a decrease in repetitions and an increase in time between loading sessions was not detrimental to earlier bone gains.

In our work at the Oregon State University Bone Research Laboratory (BRL), we used the dose-response approach in randomized controlled studies of a defined jumping program in prepubertal children (BRL, 2003). We held the loading stimulus constant and manipulated repetitions. In cohort 1, after 7 months of jumping from 2-ft boxes, 300 times per week, hip and spine BMC were higher in jumpers than controls. In a subsequent year, we performed the same randomized experiment in a separate cohort except we reduced repetitions from 300 to 150 jumps per week and, after 8 months found that there was no bone response at either the hip or the spine in prepubertal children. However, there were cohort differences, specifically, cohort 2 grew more than cohort 1. Because of these differences, we conducted an ANCOVA to answer the questions about the cohort-related differences in growth and in the bone response to jumping exercise. The greater growth in cohort 2 was independent of the longer duration of follow-up time between pre- and post-intervention assessments in cohort 2. The greater growth in cohort 2 was also independent of initial values in each growth variable. Most importantly, the greater bone response to jumping in cohort 1 was independent of cohort-related differences in initial bone values, length of follow-up duration, and growth. Therefore, the difference in jumping protocols between cohorts 1 and 2 is the only explanation for the differential bone response to jumping that cannot be excluded by the analyses. These data indicate an important synergy between repetitions and load stimulus to be answered by additional dose-response interventions.

In a study of collegiate novice and experienced rowers, we investigated whether experienced rowers gain more spine BMD over 6 months than novice rowers[32]. We hypothesized that the experienced group (n=16) would gain more bone than novices (n=19) as experienced rowers could generate higher forces over a full 6-month observation period. Since this was an observational study, we didn't actually manipulate dose, rather it was more a convenience sample in a first look at studying the effect of different load magnitudes on

bone mass changes in the spine. Each group rowed 6 times per week for approximately 90 minutes (1000-1200 strokes per session). Experienced rowers had faster times on the 2000- and 6000-meter rowing ergometer tests conducted three times at one-month intervals suggesting that the intensity variable was greater in experienced rowers compared to novices. In addition, the experienced rowers demonstrated a 2.5% increase in spine BMD that was significantly different than that of the novice rowers. Thus, a randomized controlled study investigating a difference in loading stimulus (load magnitude or loading rate) during one movement pattern such as rowing could prove to provide valuable points on the dose-response surface of the spine.

To promote compliance and long-term adherence, we must determine the minimum dose required to maintain healthy bones. An ideal exercise program would be something simple that requires little time, minimal equipment and thus does not pose a new time commitment. The overall goal is to identify programs that are all-inclusive and promote general cardiovascular and muscular health in addition to bone health. However, we will not know how to specifically increase bone mass through exercise without using carefully designed dose-response studies with clearly defined and quantified site-specific intensity variables.

References

1. National Osteoporosis Foundation, America's Bone Health: The State of Osteoporosis and Low Bone Mass in Our Nation. 2002.
2. Drinkwater BL. C.H. McCloy Research Lecture: does physical activity play a role in preventing osteoporosis? Res Q Exerc Sport 1994; 65:197-206.
3. Courtney AC, Wachtel EF, Myers ER, Hayes WC. Age-related reductions in the strength of the femur tested in a fall-loading configuration. J Bone Joint Surg Am 1995; 77:387-395.
4. Carter DR, Vasu R, Harris WH. The plated femur: relationships between the changes in bone stresses and bone loss. Acta Orthop Scand 1981; 52:241-248.
5. Snow-Harter C, Whalen R, Myburgh K, Arnaud S, Marcus R. Bone mineral density, muscle strength, and recreational exercise in men. J Bone Miner Res 1992; 7:1291-1296.
6. Taaffe DR, Robinson TL, Snow CM, Marcus R. High-impact exercise promotes bone gain in well-trained female athletes. J Bone Miner Res 1997; 12:255-260.
7. Kannus P, Haapasalo H, Sankelo M, Sievanen H, Pasanen M, Heinonen A, Oja P, Vuori I. Effect of starting age of physical activity on bone mass in the dominant arm of tennis and squash players. Ann Intern Med 1995; 123:27-31.
8. Fuchs RK, Snow CM. Gains in hip bone mass from high-impact training are maintained: a randomized controlled trial in children. J Pediatr 2002; 141:357-362.
9. Ulrich CM, Georgiou CC, Gillis DE, Snow CM. Lifetime physical activity is associated with bone mineral density in premenopausal women. J Womens Health 1999; 8:365-375.
10. Turner CH. Three rules for bone adaptation to mechanical stimuli. Bone 1998; 23:399-407.
11. Bauer JJ, Fuchs RK, Smith GA, Snow CM. Quantifying force magnitude and loading rate from drop landings that induce osteogenesis. J Appl Biomech 2001; 17:142-152.
12. Snow CM, Shaw JM, Winters KM, Witzke KA. Long-term exercise using weighted vests prevents hip bone loss in postmenopausal women. J Gerontol A Biol Sci Med Sci 2000; 55:M489-M491.
13. Winters KM, Snow CM. Detraining reverses positive effects of exercise on the musculoskeletal system in premenopausal women. J Bone Miner Res 2000; 15:2495-2503.
14. Bassey EJ, Rothwell MC, Littlewood JJ, Pye DW. Pre- and postmenopausal women have different bone mineral density responses to the same high-impact exercise. J Bone Miner Res 1998; 13:1805-1813.
15. Snow CM, Williams DP, LaRiviere J, Fuchs RK, Robinson TL. Bone gains and losses follow seasonal training and detraining in gymnasts. Calcif Tissue Int 2001; 69:7-12.
16. Cullen DM, Smith RT, Akhter M.P. Bone-loading response varies with strain magnitude and cycle number. J Appl Physiol 2001; 91:1971-1976.
17. Hsieh YF, Robling AG, Ambrosius WT, Burr DB, Turner CH. Mechanical loading of diaphyseal bone *in vivo*: the strain threshold for an osteogenic response varies with location. J Bone Miner Res 2001; 16:2291-2297.
18. Hsieh YF, Turner CH. Effects of loading frequency on mechanically induced bone formation. J Bone Miner Res 2001; 16:918-924.
19. Robling AG, Hinant FM, Burr DB, Turner CH. Shorter, more frequent mechanical loading sessions enhance bone mass. Med Sci Sports Exerc 2002; 34:196-202.
20. Robling AG, Hinant FM, Burr DB, Turner CH. Improved bone structure and strength after long-term mechanical loading is greatest if loading is separated into short bouts. J Bone Miner Res 2002; 17:1545-1554.
21. Robling AG, Burr DB, Turner CH. Recovery periods restore mechanosensitivity to dynamically loaded bone. J Exp Biol 2001; 204:3389-3399.
22. Robling AG, Burr DB, Turner CH. Partitioning a daily mechanical stimulus into discrete loading bouts improves the osteogenic response to loading. J Bone Miner Res 2000; 15:1596-1602.
23. Kontulainen S, Kannus P, Haapasalo H, Sievanen H, Pasanen M, Heinonen A, Oja P, Vuori I. Good maintenance of exercise-induced bone gain with decreased training of female tennis and squash players: a prospective 5-year follow-up study of young and old starters and

controls. J Bone Miner Res 2001; 16:195-201.
24. Kohrt WM, Ehsani AA, Birge SJ Jr. Effects of exercise involving predominantly either joint-reaction or ground-reaction forces on bone mineral density in older women. J Bone Miner Res 1997; 12:1253-1261.
25. Lohman T, Going S, Pamenter R, Hall M, Boyden T, Houtkooper L, Ritenbaugh C, Bare L, Hill A, Aickin M. Effects of resistance training on regional and total bone mineral density in premenopausal women: a randomized prospective study. J Bone Miner Res 1995; 10:1015-1024.
26. Nelson ME, Fiatarone MA, Morganti CM, Trice I, Greenberg RA, Evans W.J. Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures. A randomized controlled trial. JAMA 1994; 272:1909-1914.
27. Pruitt LA, Jackson RD, Bartels RL, Lehnhard HJ. Weight-training effects on bone mineral density in early postmenopausal women. J Bone Miner Res 1992; 7:179-185.
28. Heinonen A, Oja P, Sievanen H, Pasanen M, Vuori I. Effect of two training regimens on bone mineral density in healthy perimenopausal women: a randomized controlled trial. J Bone Miner Res 1998; 13:483-490.
29. Kerr D, Morton A, Dick I, Prince R. Exercise effects on bone mass in postmenopausal women are site-specific and load-dependent. J Bone Miner Res 1996; 11:218-225.
30. Kerr D, Ackland T, Maslen B, Morton A, Prince R. Resistance training over 2 years increases bone mass in calcium-replete postmenopausal women. J Bone Miner Res 2001; 16:175-181.
31. Kohrt WM, Snead DB, Slatopolsky E, Birge SJ Jr. Additive effects of weight-bearing exercise and estrogen on bone mineral density in older women. J Bone Miner Res 1995; 10:1303-1311.
32. LaRiviere J, Robinson TL, Snow CM. Spine BMD increases in experienced but not novice collegiate female rowers. Med Sci Sports Exerc 2003; (in press).