TITLE: Can Specific Loading through Exercise Impart Healing or Regeneration of the Intervertebral Disc?

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CONTRIBUTORSHIP STATEMENT

All listed authors contributions include the conception and design, acquisition of data or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, and final approval of the version published. Regarding responsibility for overall content, the lead author, James Steele, is the guarantor.

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ABSTRACT

Background Context: Low back pain (LBP) is highly prevalent and presents an enormous cost both through direct healthcare and indirectly through significant work and production loss. LBP is acknowledged widely to be a multifactorial pathology with a variety of symptoms, dysfunctions and a number of possible sources of pain. One source that has been suspected and evidenced for some time are the intervertebral discs. Some degree of disc degeneration is a physiologic process associated with aging, however, more severe degeneration and/or structural abnormality may be indicative of a pathological process or injury, and is more commonly present in those suffering from LBP. Much like other tissue's (i.e. muscle, bone etc.) it has been suspected that there exists an optimal loading strategy to promote the health of the disc. Exercise is often prescribed for LBP and effectively reduces pain and disability. However, whether specific loading through exercise might plausibly heal or regenerate the intervertebral discs is unknown.

Purpose: Thus the purpose of this brief review was to examine the effects of loading upon regenerative processes in the intervertebral disc and consider the potential for specific exercise to apply loading to the lumbar spine to produce these effects.

Study Design: A brief narrative literature review

Methods: Studies examining the effects of loading upon the intervertebral discs were reviewed to examine the plausibility of using loading through exercise to induce regeneration or healing of the intervertebral disc.

Results: Research from animal model studies suggests the existence of a dose-response relationship between loading and regenerative processes. Though high loading at high volumes and frequencies might accelerate degeneration or produce disc injury, high loading, yet of low volume and at low frequency appears to induce potentially regenerative mechanisms including improvements in disc proteoglycan content, matrix gene expression, rate of cell apoptosis and improved fluid flow and solute transport.

Conclusions: Research suggests a dose-response relationship between loading and disc regenerative processes and that the loading pattern typically utilised in lumbar extension resistance exercise interventions (high load, low volume, low frequency) might impart healing or regeneration of the intervertebral discs. Future research should examine an exercise intervention with *in vivo* measurement of changes in disc condition. This may provide further evidence for the 'black box' of treatment mechanisms associated with exercise interventions.

Introduction & Background

Low back pain (LBP) is one of the most prevalent medical disorders in society [1-4] and causes significant suffering for many. It presents a cost of billions worldwide (~£5-10 billion UK [5]; ~$100-200 billion USA [6]), including extensive direct healthcare costs [5-7], and indirect costs through work and production losses (~50-149 million work-days lost [8,9]. LBP is acknowledged as a multifactorial pathology presenting a wide variety of physical symptoms and dysfunctions, some of which may be causative, and others which may be symptoms of underlying dysfunction [10,11].

The intervertebral discs, however, have been suspected to be a potential source of painful symptoms in LBP for some time [12] and there is much well documented supporting evidence regarding mechanisms for how pain may occur [13,14]. Despite the disc being a potential source of pain, in addition to the many biologically plausible mechanisms which might instigate a pain response, there is some disparity in the literature linking the presence of LBP to disc abnormality. Magnetic resonance imaging (MRI) [15-20], radiography [21], and discography [22,23] have all suggested that disc abnormalities can be present in asymptomatic participants, which has brought into question the likelihood of these findings in symptomatic patients holding clinical relevance to the pain they are experiencing. However, recent literature highlights that although it may be difficult to attribute specific disc pathologies to LBP on an individual basis, there are consistent associations of certain disc abnormalities (i.e. high intensity zone (HIZ), degree of disc degeneration, disc herniation and nerve root deviation/compression) in those who suffer from LBP [24-26].

It should be considered also that the subsequent pain response after injury is in part dependent upon severity [27]. In the case of abnormalities in asymptomatic participants it may be that a threshold of degeneration/injury may not have been achieved to initiate a pain causing mechanism. Thus, examination of the literature should consider the severity of degeneration as it relates to LBP. Adams and Roughley [13] suggest the presence of some degree of degeneration is a physiologic process associated with aging, whereas more severe degeneration and/or structural abnormality may be indicative of a pathological process or injury and more commonly present in those suffering from LBP. Many studies support the contention that more severe degrees of degeneration and/or structural abnormality are more consistently apparent in participants with LBP than those who are asymptomatic [16,17,22,23,28] in a dose dependent manner [29,30]. Even if not all disc abnormalities can be ascribed as the source of LBP, any degenerative changes also heighten the risk for more severe disc degeneration or injury and thus pain and suffering [14]. Thus it seems that, as a consistent finding in symptomatic participants, and a potential source of pain symptoms, disc degeneration or injury is a worthwhile factor to consider in treatment of LBP. Exercise is a common prescription for those with LBP; however, the potential for it to specifically promote positive changes in the intervertebral discs is not often considered.

Loading, Exercise and its Effect on the Disc

Biochemical analysis of the changes involved in symptomatic degenerative discs compared to asymptomatic discs shows that significant metabolic abnormalities are present including; reduced glycosaminoglycans, dehydration, and reduced nucleas pulposus pH [31]. Some have suggested that such metabolic abnormalities in the intervertebral disc might be improved, thus potentially halting or reversing the degenerative process, through appropriate loading of the lumbar spine through exercise [32,33]. However, not all exercises are equally effective in loading and exercising the lumbar spine. A recent review has suggested that the use of isolated lumbar extension (ILEX) may be the most effective exercise for this purpose [34]. Thus it might be considered the most likely candidate for potentially improving disc condition also. Indeed, studies performing ILEX resistance exercise show successful rehabilitation outcomes in terms of pain and disability in participants with diagnosis of degenerative discs [35,36]. In addition, significantly favourable outcomes for participants undergoing lumbar discectomy for disc herniation have been shown as a result of ILEX exercise [37]. Other studies using compound trunk extension training also suggest that the presence of severe disc degeneration at the least has no negative influence on the efficacy of treatment [38].

Despite these findings, there is some opposition to the use of loaded extension based exercise in LBP for fear of causing further damage to the discs [39]. It is suggested that excessive cycles of flexion-extension under a high compressive load may increase the risk of disc herniation [39,40]. The use of ILEX in rehabilitation consists of progressive resistance exercise to train the isolated muscles that extend the lower back [41]. This type of training has been considered therefore to involve increased risk of disk herniation [39]. However the rehabilitation performed typically consists of relatively short times under loading and infrequent training sessions. In contrast, Callaghan and McGill [40] found that the number of flexion-extension cycles was more highly related to disc herniation (upward of 5000 cycles at differing loads). ILEX exercise rehabilitation typically utilises a resistance that will elicit approximately ~8-12 repetitions, and at most around 15 repetitions, before achieving momentary muscular failure using a repetition duration $\geq$7 seconds [41]. Therefore the risk of herniation may not be as great as suggested. There is also concern however that excessive loading may increase rate of disc cell apoptosis [39,42] and may therefore contribute to the inflammatory process by which disc degeneration occurs. However, citing research by Lotz and Chin [42] may be questionable in concluding that excessive loading is responsible for increased apoptosis in this context because the compressive loadings used in this study were applied for periods ranging from 1 to 7 days. In fact, Lotz and Chin's [42] results showed that the degree of apoptosis was proportional to duration of loading; thus longer exposure presented greater risk. As explained, the treatment protocol used with ILEX avoids such sustained loading (through low repetition ranges and frequency of exercise).

Reviews of the literature suggest the potential for a "safe window" of disc loading to exist that may stimulate optimal disc health [43,44]. Evidence suggesting loaded ILEX exercise as being effective in LBP even when disc degeneration is present has been highlighted [35,36]. Although some studies discussed [40,42] have been interpreted [39] to suggest it could potentially present a risk to the disc, a number of further studies using animal models provide evidence instead for a potential beneficial effect of mechanical loading upon disc degenerative processes, demonstrating biological plausibility for the concept of ILEX resistance exercise for improving disc health.

Earlier studies have suggested that continued compressive loading can contribute to harmful responses in the disc in a dose-dependent manner (i.e. magnitude and duration), which might further suggest cause for concern in employing ILEX resistance exercise for those with LBP [45,46]. However, this dose-dependent mechanism has important implications for ILEX resistance exercise, which is also typically employed in a dose-dependent manner. As explained, ILEX rehabilitation selects a resistance that allows only ~8-12 repetitions and exercise is performed to momentary muscular failure using this resistance, which has been suggested as optimal for strength and hypertrophic adaptations [47,48]. An exercise frequency of once per week has also been identified as sufficient for improving lumbar extension strength, pain and disability [49,50]. Thus ILEX rehabilitation represents a relatively high loading on the disc though at a low frequency and volume. Walsh and Lotz [51] report that, in comparison to higher frequency and lower load compression, lower frequency and higher load compression induces positive improvements in disc proteoglycan content, matrix gene expression and rate of cell apoptosis. Thus there may be potential for ILEX rehabilitation to exert a similar adaptive effect. Indeed, Maclean et al. [52,53] have also showed that anabolic and catabolic responses in the nucleus are dependent upon load and frequency with anabolic genes being stimulated at low frequencies and catabolic genes being stimulated at higher frequencies. They also revealed that very low loading had no effect upon gene expression suggesting that some degree of loading, though at a low frequency, is required to stimulate an adaptive anabolic response.

These studies have examined what might be considered regenerative processes, but as we have highlighted, a loss of disc hydration is also present in degenerative discs [31] and so rehydration may also be an important consideration. Ferguson et al. [54] have shown that loading increases fluid flow across the disc, which in turn also enhances transport of larger solutes into the intervertebral disc. ILEX rehabilitation may enhance pressure variance across the disc through its flexion-extension cycles and thus enhance interstitial fluid flow [50]. The findings of Ferguson et al. [54] would lend biological plausibility to this potential mechanism also. A last addition to this discussion of biological plausibility considers the type of loading upon the disc. ILEX typically utilises a dynamic exercise and Wang et al. [55] have presented that while static loading contributes to catabolic activity, dynamic compressive loading contrastingly promotes anabolic activity.

Specific Loading through Exercise May Improve Disc Condition

It is apparent that the intervertebral disc represents a potential source of pain and that disc degeneration is a common factor in LBP. It also seems that ILEX exercise is successful in rehabilitation outcomes even in the presence of such degeneration in symptomatic participants, despite concerns by some authors. As such it seems reasonable to hypothesise that such exercise may in fact impart a healing or perhaps regenerative adaptation to the disc itself. The concept of applied loading in order to promote tissue healing in musculoskeletal conditions (i.e. Mechanotherapy) has been revisited in recent years [56] Indeed as we have discussed, there is significant evidence from animal models to provide biological plausibility for how such an adaptation might occur in the intervertebral discs.

Research has also shown that improvements in both lumbar extensor muscle condition [37,57] and lumbar bone mineral density are produced through ILEX rehabilitation [58-63]. These results might suggest that a sufficient degree of specific loading may be required to promote a positive adaptive response in muscle, bone, and thus potentially the disc also. Indeed epidemiological evidence also suggests that strength training and bodybuilding results in a lowered risk of disc degeneration [64]. Thus we hypothesise that specific loading through ILEX exercise may possibly impart an adaptive response and healing or regeneration of the intervertebral disc.

It has been suggested that therapeutic pharmacologic interventions could possibly instigate regeneration of the intervertebral disc [65,66] but, despite suggestions for therapeutic loading strategies [43,44,46] the effects of exercise upon disc condition *in vivo* have not been investigated through means of a randomised controlled trial. Adams et al. [14] have recently reviewed the potential for healing to occur in the symptomatic intervertebral disc and suggested that potential mechanisms for disc reparation will likely predominantly involve the annulus. Being that this is an area yet to be examined fully *in vivo*, and that as suggested here there may be mechanisms of positive adaptation in both the annulus and nucleus, we suggest that any study seeking to test this hypothesis should invariably look to examine all possible aspects of disc condition.

Taken collectively the evidence highlights potential for ILEX exercise rehabilitation to produce beneficial adaptation in the intervertebral discs of symptomatic participants. It also seems apparent that there may be an optimal dose (load, duration, frequency) for which these adaptations are produced. However, these potential adaptations have yet to be investigated *in vivo* through use of MRI. Thus we suggest that in order to test the hypothesis that “specific loading applied through use of ILEX resistance exercise can impart healing or regeneration of the intervertebral disc” be examined through means of a randomised controlled trial to examine *in vivo* changes in disc condition. The intervention used in the trial should follow typical recommendations for ILEX rehabilitation as used in recent studies of ILEX [50,67,68] and could be investigated in both participants with diagnosed disc degeneration and/or injury, in addition to those with non-specific LBP. Ideally the outcome measure used would be MRI and a range of possible factors indicating disc condition be considered for changes using standard validated means of assessment.

We believe further study of this kind might provide a robust test of this hypothesis and may offer some further insight into the ‘black box’ of mechanisms of exercise interventions effects in LBP [69]. Should the hypothesis be found to be supported then future work might consider comparative studies of interventions, both exercise and other, to examine relative efficacy. However, considering the multifactorial nature of LBP, if an intervention such as ILEX is found to induce positive adaptation in the intervertebral disc this might be considered as representing further cost effectiveness to the approach due to the wide range of positive outcomes that might be possible from such a minimal single intervention [70].

References

1. World Health Organisation (WHO). The World Health Report 1998: Life in the 21st century: A vision for all. Geneva: Office of Publications, World Health Organisation; 1998
2. Waddell G, Burton AK. Occupational health guidelines for the management of low back pain at work: evidence review. Occup Med 2001;51:126–135
3. Walker BF. The prevalence of low back pain: a systematic review of the literature from 1966 to 1998. J Spinal Disord 2000;13(3):205–217
4. National Institute for Health and Clinical Excellence (NICE). Low back pain: early management of persistent non-specific low back pain. London: Royal College of General Practitioners; 2009
5. Maniadakis N, Gray A. The economic burden of back pain in the UK. Pain 2000;84 (1):95–103.
6. Katz JN. Lumbar disc disorders and low back pain: socioeconomic factors and consequences. J Bone Joint Surg Am 2006;88(suppl 2):21–24
7. Van Tulder MW, Koes BW, Bouter LM. A cost-of-illness study of back pain in The Netherlands. Pain 1995;62(2):233–240
8. Guo HR, Tanaka S, Halperin WE, Cameron LL. Back pain prevalence in US industry and estimates of lost workdays. Am J Public Health 1999;89:1029–1035
9. Waddell G, Aylward M, Sawney P. Back Pain, incapacity for work and social security benefits: an international literature review and analysis. Glasgow: The Royal Society of Medicine Press Ltd; 2002
10. National Research Council (NRC). Work-related musculoskeletal disorders: A Review of the evidence. National Academy Press: Washington, DC; 1998
11. National Research Council (NRC), and The Institute of Medicine (IOM). Musculoskeletal disorders and the workplace: Low back and upper extremities. National Academy Press: Washington, DC; 2001
12. Mixter WJ, Barr JS. Rupture of the intervertebral disc with involvement of the spinal canal. N Eng J Med 1934;211:210–215
13. Adams MA, Roughley PJ. What is intervertebral disc degeneration, and what causes it? Spine 2006;31(18):2151–2161

14. Adams MA, Stefanakis M, Dolan P. Healing of a painful intervertebral disc should not be confused with reversing disc degeneration: implications for physical therapies for discogenic back pain. Clin Biomech 2010;25:961–971
15. Boden SD, Davis DO, Dina TS, Patronas NJ, Wiesel SW. Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects. A prospective investigation. J Bone Joint Surg 1990;72:403–408
16. Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, Ross JS. Magnetic resonance imaging of the lumbar spine in people without back pain. N Engl J Med 1994;331(2):69–73
17. Weishaupt D, Zanetti M, Hodler J, Boos N. MR imaging of the lumbar spine: prevalence of intervertebral disk extrusion and sequestration, nerve root compression, end plate abnormalities and osteoarthritis of the facet joints in asymptomatic volunteers. Radiology 1998;209(3):661-669
18. Borenstein DG, O'Mara J, Boden SD, Lauerman WC, Jacobson A, Platenberg C, Schellinger D, Wiesel SW. The value of magnetic resonance imaging of the lumbar spine to predict low back pain in asymptomatic subjects. J Bone Joint Surg 2001;83(9):1306–1311
19. Barento A, Hellström M, Cederlund CG, Nyman R, Sward L. Back pain and MRI changes in the thoraco-lumbar spine of top athletes in four different sports: a 15 year follow-up study. Knee Surgery, Sports Traumatology. Arthroscopy 2009;17:1125–1134
20. Maurer M, Soder RB, Baldisserotto M. Spine abnormalities depicted by magnetic resonance imaging in adolescent rowers. Am J Sports Med 2011;39(2):392–397
21. Iwamoto J, Abe H, Tsukimura Y, Wakano K. Relationship between radiographic abnormalities of lumbar spine and incidence of low back pain in high school rugby players: a prospective study. Scand J Med Sci Sports 2005;15:163–168
22. Holt EP. The question of lumbar discography. J Bone Joint Surg 1968;50:720–726
23. Walsh TR, Weinstein JN, Spratt KF, Lehmann TR, Aprill C, Sayre H. Lumbar discography in normal subjects. A controlled, prospective study. J Bone Joint Surg 1990;72:1081–1088
24. Endean A, Palmer KT, Coggon D. Potential of magnetic resonance imaging findings to refine case definition for mechanical low back pain in epidemiological studies. Spine 2011;36(2):160–169
25. McNee P, Shambrook J, Harris EC, Sampson M, Palmer KT, Coggon D. Predictors of long-term pain and disability in patients with low back pain investigated by magnetic resonance imaging: A longitudinal study. BMC Musculoskelet Disord 2011;12:234

26. Shambrook J, McNee P, Harris EC, Kim M, Sampson M, Palmer KT, Coggon D. Clinical presentation of low back pain and association with risk factors according to findings on magnetic resonance imaging. Pain 2011;152:1659–1665
27. DeLeo JA, Winkelstein BA. Physiology of chronic spinal pain syndromes: From animal models to biomechanics. Spine 2002;27:2526–2537
28. Kjaer P, Leboeuf-Yde C, Kowsholm L, Sorenson JS, Bendix T. Magnetic resonance imaging and low back pain in adults: a diagnostic study of 40 year old men and women. Spine 2005;30(10):1173–1180
29. Cheung KMC, Karppinen J, Chan D, Ho DWH, Song Y, Sham P, Cheah KSE, Leong JCY, Luk KDK. Prevalence and pattern of lumbar magnetic resonance imaging changes in a population study of one thousand forty-three individuals. Spine 2009;34(9):934–940
30. de Schepper EIT, Damen J, van Meurs JBJ, Ginai AZ, Popham M, Hofman A, Koes BW, Bierma-Zeinstra SM. The association between lumbar disc degeneration and low back pain. Spine 2010;35(5):531–536
31. Kitano T, Zerwekh JE, Usui Y, Edwards ML, Flicker PL, Mooney V. Biochemical changes associated with the symptomatic human intervertebral disk. Clin Orthop Relat Res 1993;293:372–377
32. Mooney V, Verna J, Morris C. Clinical management of chronic, disabling low back syndromes. In. Morris C, ed. Rehabilitation of the Spine: A Practitiioners Manual. New York: McGraw-Hill; 2006
33. Mayer J, Mooney V, Dagenais S. Evidence informed management of chronic low back pain with lumbar extensor strengthening exercises. Spine J 2008;8:96–113
34. Steele J, Bruce-Low S, Smith D. A review of the specificity of exercises designed for conditioning the lumbar extensors. Br J Sports Med. Online First
35. Highland TR, Dreisinger TE. Degenerative disc disease in a collegiate volleyball player. Med Sci Sports Exerc 1992;24(5):S163
36. Nelson BW, O'Reilly E, Miller M. The clinical effects of intensive, specific exercise on low back pain: A controlled study of 895 consecutive patients with a one year follow up. Orthopedics 1995;18(10):971–981.
37. Choi G, Raiturker PP, Kim MJ, Jin CD, Chae YS. The effect of early isolated lumbar extension exercise program for patients with herniated disc and undergoing lumbar discectomy. Neurosurgery 2005;57(4):764–772

38. Kleinstuck F, Dvorak J, Mannion AF. Are “structural abnormalities” on magnetic resosnance imaging a contraindication to the successful conservative treatment of chronic nonspecific low back pain? Spine 2006;31(19):2250–2257

39. McGill SM. Low back disorders: evidence-based rehabilitation and prevention. 2nd ed. Human Kinetics: Champaign; 2007

40. Callaghan JP, McGill SM. Intervertebral disc herniation: studies on a porcine model exposed to highly repetitive flexion/extension motion with compressive force. Clin Biomech 2001;16(1):28–37

41. Smith D, Bruce-Low S, Bissell G. Twenty years of specific, isolated lumbar extension research: A review. J Orthop 2011;5(1):e14

42. Lotz JC, Chin JR. Intervertebral disc cell death is dependent on the magnitude and duration of spinal loading. Spine 2000;25(12):1477–1483

43. Stokes IAF, Iatridis JC. Mechanical conditions that accelerate intervertebral disc degeneration: Overload versus immobilization. Spine 2004;29(23):2724–2732

44. Chan ACW, Ferguson SJ, Gantenbein-Ritter B. The effects of dynamic loading on the intervertebral disc. Eur Spine J 2011;20:1796–1812

45. Lotz JC, Colliou OK, Chin JR, Duncan NA, Lienbenberg E. Compression-induced degeneration of the intervertebral disc: and in vivo mouse model and finite-element study. Spine 1998;23(23):2493–2506

46. Kroeber MW, Unglaub F, Wang H, Schmid C, Thomsen M, Nerlich A, Richter W. New in vivo animal model to create intervertebral disc degeneration and to investigate the effects of therapeutic strategies to stimulate disc regeneration. Spine 2002;27(23):2684–2690

47. Fisher J, Steele J, Bruce-Low S, Smith D. Evidence based resistance training recommendations. Med Sport 2011;15(3):147–162

48. Fisher J, Steele J, Smith D. Evidence based resistance training recommendations for muscular hypertrophy. Med Sport 2013;17(4):217–235

49. Graves JE, Pollock ML, Foster D, Leggett SH, Carpenter DM, Vuoso R, Jones A. Effect of training frequency and specificity on isometric lumbar extension strength. Spine 1990;15(6):504–509

50. Bruce-Low S, Smith D, Burnett S, Fisher J, Bissell G, Webster L. One lumbar extension training session per week is sufficient for strength gains and reductions in pain in patients with chronic low back pain ergonomics. Ergonomics 2012;55(4):500–507

51. Walsh AJ, Lotz JC. Biological response of the intervertebral disc to dynamic loading. J Biomech 2004;37(3):329–337
52. Maclean JJ, Lee CR, Alini M, Iatridis JC. Anabolic and catabolic mRNA levels of the intervertebral disc vary with the magnitude and frequency of in vivo dynamic compression. J Orthop Res 2004;22(6):1193–1200
53. Maclean JJ, Lee CR, Alini M, Iatridis JC. The effects of short-term load duration on anabolic and catabolic gene expression in the rat tail intervertebral disc. J Orthop Res 2005;23(5):1120-1127
54. Ferguson SJ, Ito K, Nolte LP. Fluid flow and convective transport of solutes within the intervertebral disc. J Biomech 2004;37(2):213–221
55. Wang DL, Jiang SD, Dai LY. Biologic response of the intervertebral disc to static and dynamic compression in vitro. Spine 2007;32(23):2521–2528
56. Khan KM, Scott A. Mechanotherapy: how physical therapists' prescription of exercise promotes tissue repair. Br J Sports Med 2009;43:247–251
57. Mooney V, Gulick J, Perlman M, Levy D, Pozos R, Leggett S, Resnick D. Relationships between myoelectric activity, strength and MRI of lumbar extensor muscles in back pain patients and normal subjects. J Spinal Disord 1997;10(4):348–356
58. Pollock ML, Gazarella L, Graves JE, Carpenter DM, Leggett SH, Lowenthal D, Fulton MN, Foster D, Tucci J, Mananquil RR. Effects of isolated lumbar extension resistance training on bone mineral density of the elderly. Med Sci Sports Exerc 1992;24(5):S66
59. Braith RW, Mills RM, Welsch MA, Keller JW, Pollock ML. Resistance exercise training restores bone mineral density in heart transplant recipients. J Am Coll Cardiol 1996;28(6):1471–1477
60. Braith RW, Magyari PM, Fulton MN, Aranda J, Walker T, Hill JA. Resistance exercise training and alendronate reverse glucocorticoid-induced osteoporosis in heart transplant recipients. J Heart Lung Transplant 2003;22(10):1082–1090
61. Mitchell MJ, Baz MA, Fulton MN, Lisor CF, Braith RW. Resistance training prevents vertebral osteoporosis in lung transplant recipients. Transplantation 2003;76(3):557–562
62. Braith RW, Magyari PM, Fulton MN, Lisor CF, Vogel SE, Hill JA, Aranda JM. Comparison of calcitonin versus calcitonin + resistance exercise as prophylaxis for osteoporosis in heart transplant recipients. Transplantation 2006;81(8):1191–1195

63. Braith RW, Conner JA, Fulton MN, Lisor CF, Casey DP, Howe KS, Baz MA. Comparison of Alendronate vs Alendronate plus mechanical loading as prophylaxis for osteoporosis in lung transplant recipients: a pilot study. J Heart Lung Transplant 2007;26(2):132–137
64. Schumann B, Bolm-Audorff U, Bergmann A, Ellegast R, Elsner G, Grifka J, Haerting J, Jager M, Michaelis M, Seidler A. Lifestyle factors and lumbar disc disease: results of a German multi-center case-control study (EPILIFT). Arthritis Res Ther 2010;12(5):R193
65. Ireland D. Molecular mechanisms involved in intervertebral disc degeneration and potential new treatment strategies. Bioscience Horizons 2009;2(1):83–89
66. Smith LJ, Nerurkar NL, Choi K, Harfe BD, Elliot DM. Degeneration and regeneration of the intervertebral disc: lessons from development. Dis Model Mech 2011;4(1):31–41
67. Smith D, Bissell G, Bruce-Low S, Wakefield C. The effect of lumbar extension training with and without pelvic stabilization on lumbar strength and low back pain. J Back Musculoskelet Rehabil 2011;24:1–9
68. Steele J, Bruce-Low S, Smith S, Jessop D, Osborne N. A Randomised Controlled Trial of Limited Range of Motion Lumbar Extension Exercise in Chronic Low Back Pain. Spine 2013;38(15):1245–1252
69. Helmhout PH, Staal JB, Maher CG, Petersen T, Rainville J, Shaw WS. Exercise therapy and low back pain: Insights and proposals to improve the design, conduct, and reporting of clinical trials. Spine 2008;33(16):1782-1788
70. Helmhout PH, Harts C, Staal JB, de Bie RA. Rationale and design of a multicentre randomized controlled trial on a ‘minimal intervention’ in Dutch army personnel with nonspecific low back pain. BMC Musculoskelet Disord 2004;5:40