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|  |  |
| --- | --- |
| Code | Intervention |
| 1 | Placebo |
| 2 | Teriparatide |
| 3 | Denosumab |
| 4 | Raloxifene |
| 5 | Zoledronate |
| 6 | Risedronate |
| 7 | Ibandronate |
| 8 | Alendronate |
| 9 | Vitamin D |
| 10 | Vitamin D+Calcium |
| 11 | Calcium |
| 12 | Bazedoxifene |
| 13 | Hormone therapy |
| 14 | Tibolone |
| 15 | Strontium ranelate |
| 16 | Lasofoxifene |
| 17 | Calcitonin |
| 18 | Romosozumab |
| 19 | Abaloparatide |

# S**upplemental Figure 1. Network of hip fracture trials**

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# S**upplemental Figure 2. Network of nonvertebral fracture trials**

|  |  |
| --- | --- |
| Code | Intervention |
| 1 | Placebo |
| 2 | Teriparatide |
| 3 | Denosumab |
| 4 | Raloxifene |
| 5 | Zoledronate |
| 6 | Risedronate |
| 7 | Ibandronate |
| 8 | Alendronate |
| 9 | Strontium ranelate |
| 10 | Vitamin D+Calcium |
| 11 | Bazedoxifene |
| 12 | Tibolone |
| 13 | Hormone therapy |
| 14 | Calcitonin |
| 15 | Lasofoxifene |
| 16 | Vitamin D |
| 17 | Calcium |
| 18 | PTH 1-84 |
| 19 | Romosozumab |
| 20 | Abaloparatide |

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# S**upplemental Figure 3. Network of vertebral fracture trials**

|  |  |
| --- | --- |
| Code | Intervention |
| 1 | Placebo |
| 2 | Teriparatide |
| 3 | Denosumab |
| 4 | Raloxifene |
| 5 | Zoledronate |
| 6 | Risedronate |
| 7 | Ibandronate |
| 8 | Alendronate |
| 9 | Vitmin D+Calcium |
| 10 | Calcium |
| 11 | Bazedoxifene |
| 12 | Lasofoxifene |
| 13 | Hormone therapy |
| 14 | Calcitonin |
| 15 | Tibolone |
| 16 | Strontium ranelate |
| 17 | PTH 1-84 |
| 18 | Vitamin D |
| 19 | Romosozumab |
| 20 | Abaloparatide |

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# Supplemental table 1: Description of the included trials

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author, Year** | **Patients description** | **Baseline BMD status** | **Age (yrs)** | **Race / Ethnicity** | **N** | **Interventions** | **Intervention duration** | **calcium** | **vit D** | **Country** |
| Alexandersen, 1999(1) | Healthy postmenopausal women with low BMD | Osteoporosis and osteopenia | 65 | NR | 50 | HRT (17β-estradiol 50 µg/day, patch + norethisterone acetate oral 1 mg/day) vs. placebo | 24 months | Both arms | Both arms | Denmark |
| Bai, 2013(2) | Postmenopausal women with Osteoposis | Osteoporosis | 56.8 | 100% asian | 483 | zoledronate 5 mg/ year vs. placebo | 24 months | Both arms | Both arms | China |
| Bischoff,2003(3) | Women aged ≥60 years with the ability to walk 3 m with or without a walking aid | NR | 84.6 | NR | 122 | vitamin D3 800 IU vs. placebo | 3 months | Both arms | No | Switzerland |
| black, 1996(4) | Women aged 55-81 years with existing vertebral fractures, with at least 2 years of menopause and low femoral-neck BMD | Osteopenia or Osteoporosis | 55-81 | 97% white, 1% asian, 1% black | 2027 | alendronate 5mg/day for 24 months and then increased to 10 mg/day vs. placebo | 36 months | Both arms | Both arms | USA |
| black, 2007(5) | Women aged 65-89 years with osteoporosis | Osteoporosis | 73 | NR | 7765 | zoledronate, 5mg / year vs. placebo | 24 months | Both arms | Both arms | Multiple countries |
| Blair, 2009(6) | Postmenopausal women with osteoporosis | Osteoporosis | 68.7 | 100% asian | 329 | calcitonin (salmon calcitonin) intranasal 200 IU/day vs. teriparatide 20 µg/day | 6 months | Both arms | Both arms | Multiple countries |
| Bock, 2012(7) | Women aged 60-75 years with menopause for >5 years with osteoporosis | Osteoporosis | NR | NR | 70 | ibandronate 150 mg/month vs. placebo | 12 months | Both arms | Both arms | Germany |
| Body, 2002(8) | Ambulatory postmenopausal women aged 30-85 years | Osteoporosis | 65.5 | 82% white | 146 | alendronate 10 mg/day vs. teriparatide 40 µg/day | 14 months | Both arms | Both arms | Multiple countries |
| Bolton-Smith, 2007(9) | Healthy women ≥60 years | Normal BMD | 68.3 | NR | 123 | vitamin D 400 IU + calcium 1 g/day vs. placebo | 24 months | No | No | UK |
| Bone, 1997(10) | Women aged 60-85 years with osteoporosis | Osteoporosis and osteopenia | 71 | 97% white | 359 | alendronate 1, 2.5 or 5 mg / day vs. placebo | 24 months | Both arms | Both arms | USA |
| Bone, 2008(11) | Ambulatory postmenopausal women with osteopenia | Osteopenia | 59.4 | 83% white | 332 | denosumab, 60 mg/6 months vs. placebo | 24 month | Both arms | Both arms | Multiple countries |
| Bush, 1996(12) | Healthy postmenopause women aged 45-64 years | Normal BMD | 56 | 88.7% white | 875 | HRT (CEE 0.625 mg/day only, or cyclic or continuous CEE 0.625 mg/day + MPA 10 mg/day [day 1 to 12], or CEE 0.625 mg/day + MPA 2.5 mg/day, or CEE 0.625 mg/day + micronized progesterone) vs. placebo | 36 months | NR | NR | USA |
| Cauley, 2003(13) | Postmenopausal women with an intact uterus | NR | 63.3 | 84% white, 7% black, %% hispanic, 0.3% native american, 2% asian/Pacific Islander | 16608 | estrogen + progestin vs. placebo | 18 months | NR | NR | USA |
| Chapuy, 1992/1994(14, 15) | Healthy women living in nursing homes or apartment houses | NR | 84 | NR | 3270 | vitamin D3 800 IU/day + tricalcium phosphate 1.2 g/day vs. placebo | 18 months | No | No | France |
| Chapuy, 2002(16) | Ambulatory women with life expectancy of at least 24 months | NR | NR | NR | 583 | vitamin D3 800 IU/day + elemental calcium 1.2 g/day as a fixed combination or separate vs. placebo | 24 months | No | No | France |
| Chesnut, 2000(17) | Postmenopausal women for at least 1 year with osteoporosis | Osteoporosis | 68.3 | white, asian, or hispanic | 1255 | calcitonin (salmon calcitonin) intranasal 100, 200, or 400 IU/day vs. placebo | 60 months | Both arms | Both arms | Multiple countries |
| Chesnut, 2004(18) | Women aged 55-80 years and ≥5 years postmenopausal with osteoporosis | Osteoporosis | 69 | NR | 2946 | ibandronate 2.5 mg/day or 20 mg in 4 doses/month vs. placebo | 36 months | Both arms | Both arms | Multiple countries |
| Clemmesen, 1997(19) | Healthy women with at least 1 year of menopause with osteoporosis | Osteoporosis | 68 | NR | 132 | risedronate 2.5 mg/day vs. placebo | 24 months | Both arms | No | Multiple countries |
| Cosman, 2009(20) | Women aged ≥50 years with osteoporosis | Osteoporosis | 68.4 | NR | 99 | alendronate 70 total mg/week vs. raloxifene 60 mg/day | 18 months | Both arms | Both arms | USA |
| Cosman, 2011(21) | Postmenopausal women with osteoporosis | Osteoporosis | 45-89 | 97.9% white | 275 | teriparatide 20 µg/day + injectable placebo vs. zoledronate 5 mg/once | 12 months | Both arms | Both arms | Multiple countries |
| Cosman, 2016(22) | Postmenopausal ambulatory women aged 55-90 years | Osteoporosis | 70.9 | 39.6% hispanic, 60.4% non-hipanic | 7180 | romosozumab sc 210 mg/month vs. placebo | 12 months | Both arms | Both arms | Multiple countries |
| Cummings, 1998(23) | Women aged 55-80 years without a vertebral fracture, with at least 2 years of menopause and BMD of 0.68 g/cm2 | Osteopenia and osteoporosis | 68 | 97% white | 4432 | alendronate 5 mg/day vs. placebo | 50.4 months | Those with Ca intakes < than 1000 mg | Those with Ca intakes < than 1000 mg | USA |
| Cummings, 2008(24) | Women aged 60-85 years with osteoporosis | Osteoporosis | 68.25 | NR | 4534 | tibolone 1.25 mg/day vs. placebo | 34 months | Both arms | Both arms | Multiple countries |
| Cummings, 2009(25) | Women aged 60-90 years with osteoporosis | Osteoporosis | 72.3 | NR | 7868 | denosumab 60 mg/6 months vs. placebo | 36 months | Both arms | Both arms | Multiple countries |
| Cummings, 2010(26) | Postmenopausal women (59 to 80 years of age) | Osteoporosis | 67 | 74.1% white, 18.4% asian | 8556 | lasofoxifene 0.25 mg/day vs. placebo | 60 months | Both arms | Both arms | Multiple countries |
| Dursun, 2001(27) | Postmenopausal women with BMD of -2 SD or less (lumbar spine or femoral neck) | Osteoporosis and osteopenia | 60.3 | NR | 101 | alendronate 10 mg/day vs. calcitonin (salmon calcitonin) intranasal 100 IU/day vs. placebo | 12 months | Yes | No | Turkey |
| Ensrud, 2008(28) | Women aged ≥55 years with documented heart disease or at high risk fo coronary events | Normal BMD | 68 | 84% white | 10101 | raloxifene 60 mg/day vs. placebo | 67.2 months (median) | NR | NR | Multiple countries |
| Ettinger, 1999(29) | Women with at least 2 years of menopause and had no severe or long-term disabling condition but osteoporosis | Osteoporosis | 67 | 95.7% white | 7705 | raloxifene 60 or 120 mg/day vs. placebo | 36 months | Both arms | Both arms | Multiple countries |
| Fogelman, 2000(30) | Women up to 80 years of age with at least 1 year of menopause and BMD -2 or less (lumbar spine) | Osteoporosis and osteopenia | 65 | NR | 359 | risedronate 5 mg/day vs. placebo | 24 months | Both arms | No | Multiple countries |
| Fogelman, 2008(31) | Postmenopausal women for a minimum of 1 year | Osteoporosis and osteopenia | 58.8 | NR | 180 | teriparatide 100 µg/day vs. placebo | 17.4 months (teriparatide), 18.2 months (placebo) | Both arms | Both arms | Multiple countries |
| Gallagher, 2001(32) | Women aged 65-77 years with normal BMD | Normal BMD | 71.7 | NR | 367 | HRT (conjugated estrogen 0.625 mg/d + MPA 2.5 mg/d) vs. vitamin D (calcitrol 0.5 µg/day) vs. placebo | 36 months | All arms | No | USA |
| Garay Lillo, 1997(33) | Ambulatory women aged 65-85 years | NR | NR | NR | 4185 | vitamin D 16,000 IU/week vs. placebo | 24 months | Both arms | No | Spain |
| Gennari, 1985(34) | Postmenopausal women with vertebral atraumatic compressions | Osteoporosis | 58.7 | NR | 45 | calcitonin (salmon calcitonin) 100 IU/day or 100IU/interdaily vs. control | 12 months | All arms | No | Italy |
| Greenspan, 1998(35) | Healthy, ambulatory, community-dwelling women aged ≥65 years | None specified | 70 | NR | 120 | alendronate 5mg (10 for the last 12 months) / day vs. placebo | 30 months | If dietary intake less than 1000 mg/d Ca | Those with low Vit. D | USA |
| Greenspan, 2002(36) | Ambulatory women aged ≥65 years living in long-term care facilities | Osteoporosis and osteopenia | 78.5 | 97% white | 327 | alendronate 10 mg/day vs. placebo | 24 months | If dietary calcium intake less than 1500 mg | Both arms | USA |
| Greenspan, 2007(37) | Postmenopausal women aged 45-54 years with osteoporosis | Osteoporosis | 64.4 | NR | 2679 | teriparatide 100 µg/day vs. placebo | 18 months | Both arms according to the patients’ needs | Both arms | Multiple countries |
| Greenspan, 2015(38) | Postmenopausal frail women aged ≥65 years who resided in a nursing home or assisted-living facility | Osteoporosis | 85.5 | NR | 181 | zoledronate 5 mg/once vs. placebo | 24 months | Both arms | Both arms | USA |
| Grey, 2009(39) | Postmenopausal women for at least 5 years with BMD between -1 and -2 (lumbar spine of total hip) | Osteopenia | 63.5 | NR | 50 | zoledronate, 5mg/once vs. placebo | 24 months | No | No | New Zealand |
| Grey, 2014(40) | Postmenopausal women for at least 5 years with BMD between -1 and -2.5 (lumbar spine of total hip) | Osteopenia | 65.3 | NR | 180 | zoledronate 1 mg, 2.5 mg or 5 mg/once vs. placebo | 24 months | No | No | New Zealand |
| Gruber, 1984(41) | Postmenopausal white women aged 51-71 years with osteoporosis | Osteoporosis | 65.4 | 100% white | 45 | calcitonin (synthetic salmon calcitonin) im or sc 100 IU/day vs. control | 24 months | Both arms | Both arms | USA |
| Hadji, 2012(42) | Women aged ≥45 years with 2 years of menopause and a history of back pain for ≥2 months | Osteoporosis | NR | 0.7% african american, 18% hispanic, 80.4% white, 0.4% asian, 0.4% native american | 710 | risedronate 35 mg/week vs teriparatide 20 µg/day | 18 months | Both arms | Both arms | USA |
| Harris, 1999(43) | Ambulatory women aged ≤85 years with at least 1 vertebral fracture | Osteoporosis | 69 | 96% white | 1641 | risedronate 5 mg/day vs. placebo | 36 months | Both arms | Those with low Vit. D | USA |
| Harwood, 2004(44) | Postmenopausal elderly women after hip fracture | Osteoporosis | 81.3 | NR | 150 | vitamin D (ergocalciferol) iv 300,000 IU/day + calcium carbonate 1 g/day vs. vitamin D 300,000 IU/day vs. control | 12 months | No | No | UK |
| Henriksen, 2016(45) | Postmenopausal ambulatory women aged 55-85 years | Osteoporosis | 66.8 | 66.5% white, 1.5% black, 19.2% hispanic, 12.8% asian | 4665 | calcitonin (salmon calcitonin) oral 0.8 mg/day vs. placebo | 36 months | Both arms | Both arms | Multiple countries |
| Hizmetli, 1998(46) | Postmenopausal women with osteoporosis | Osteoporosis | 58 | NR | 107 | calcitonin (salmon calcitonin) intranasal 50 or 100 IU/day vs. placebo | 24 months | Both arms | Both arms | Turkey |
| Hooper, 2005(47) | Early postmenopausal (6-36 months) women with osteoporosis | Osteoporosis | 53 | 98% white | 383 | Risedronate 2.5 or 5 mg/day vs. placebo | 24 months | Both arms | No | Australia |
| Hulley, 1998(48) | Posmenopause women aged 55-80 years for at least 1 year with established coronary disease | NR | 67 | 89% white | 2763 | HRT (CEE 0.625 mg/day + MPA 2.5 mg/day) vs. placebo | 36 months | NR | NR | USA |
| Ishida, 2004(49) | Ambulatory women aged 50-75 with osteoporosis | Osteoporosis | 69.5 | NR | 264 | HRT (estrogen 0.625mg/day + MPA 2.5mg/d) vs. calcitonin (eel calcitonin) 20 IU/week vs. vitamin D 1 µg/d vs. placebo | 24 months | NR | No | Japan |
| Itabashi, 2011(50) | Postmenopausal women aged ≤85 years with an intact uterus | Osteoporosis | 63 | asian | 425 | bazedoxifene 20 mg, 40 mg/day vs. placebo | 26 months | Both arms | Both arms | Japan |
| Iwamoto, 2008(51) | Postmenopausal women with osteoporosis | Osteoporosis | 69.4 | asian | 122 | alendronate 5 mg/day vs. raloxifene, 60 mg/day | 12 months | Instructed to take | No | Japan |
| Iwamoto, 2011(52) | Postmenopausal osteoporotic women with mild to moderate back pain | Osteoporosis | 79.8 | NR | 194 | alendronate 35 mg/week vs. calcitonin (as elcatonin, an eel calcitonin derivative) im 20 IU/week | 6 months | No | No | Japan |
| Jackson, 2006(53) | Postmenopausal women aged 50-79 years | NR | 62.4 | 83% white, 9.2% black, 4.2% hispanic, 0.4% american indian, 2% asian | 36282 | calcium carbonate 1 g/day + vitamin D3 400 IU/day vs. placebo | 84 months | No | No | USA |
| Jacobsen, 2012(54) | Postmenopausal women aged ≥70 years | NR | 73.7 | NR | 318 | tibolone 1.25 mg/day vs. raloxifene 60 mg/day vs. placebo | 24 months | No | No | The Netherlands |
| Koh, 2016(55) | Postmenopausal women aged 60-90 years | Osteoporosis | 66.5 | 100% asian | 135 | denosumab sc 60 mg single dose vs. placebo | 6 months | Both arms | Both arms | Korea |
| Komulainen, 1998(56) | Early postmenopausal women (6 to 24 months) | Osteoporosis | 52.5 | NR | 348 | HRT (Estradiol valerate 2 mg + cyproterone acetate 1 mg) vs. calcium 93 mg + vitamin D 300 IU/day vs. placebo | 60 months | Both arms | Both arms | Finland |
| Lees, 2001(57) | Postmenopausal women for at least 6 months and were non-hysterectomized | Normal BMD | 55.6 | NR | 579 | HRT (17β-estradiol 1 or 2 mg/day [day 1 to 28] + dydrogesterone 5, 10, or 20 mg/day [day 15 to 28]) vs. placebo | 24 months | Both arms | No | UK and Canada |
| Liberman, 1995(58) | Women aged 45-80 years with ≥5 years with menopause with osteoporosis | Osteoporosis | 64 | 87.4% white, 0.4% black; 12.2% other | 994 | alendronate 5, 10 or 20 mg/day vs. placebo | 36 months | Both arms | No | Multiple countries |
| Lindsay, 1990(59) | Postmenopausal women with osteoporosis | Osteoporosis | 62 | NR | 50 | HRT (CCE 0.625 mg/d, women with intact uterus received MPA 5-10 mg/day) vs. placebo | 24 months | Both arms | No | USA |
| Luckey, 2004(60) | Postmenopausal women aged >40 years with osteoporosis | Osteoporosis | 64.2 | 92% white | 456 | alendronate 70 mg/week vs. raloxifene 60 mg/day | 12 months | Both arms | No | USA |
| Lufkin, 1992(61) | Ambulatory postmenopausal women with osteoporosis | Osteoporosis | 64.7 | NR | 75 | HRT (Estradiol 0.1 mg/day + MPA 10 mg/day) vs. placebo | 12 months | No | No | USA |
| Lufkin, 1998(62) | Ambulatory postmenopausal women aged 45-75 years | Osteoporosis | 68.4 | NR | 143 | raloxifene 60 or 120 mg/day vs. no treatment | 12 months | Both arms | Both arms | USA |
| Macdonald, 2013(63) | Healthy postmenopausal women aged 60-70 years | Normal BMD | 64.6 | NR | 305 | vitamin D 400 or 1000 IU/day vs. placebo | 12 months | Both arms | No | UK |
| McClung, 2001(64) | Ambulatory postmenopausal women over the age of 70 | Osteoporosis | 79 | 98% white | 9331 | risedronate 2.5 or 5 mg/day vs. placebo | 24 months | Both arms | Those with low vitamin D | Multiple countries |
| McClung, 2004(65) | Healthy women >6 months postmenopause; aged <60 years | Normal BMD, Osteopenia and Osteoporosis | 55 | NR | 612 | HRT (CEE 0.625 mg/day + MPA 5 mg/day or 17β-estradiol 1-2 mg/day + norethisterone acetate 1 mg/day) vs. placebo | 72 months | No | No | Multiple countries |
| McClung, 2005(66) | Postmenopausal women aged 45-84 years with osteoporosis | Osteoporosis | 45-84 | NR | 203 | alendronate 10 mg/day + injectable placebo vs. teriparatide 20 µg/day + oral placebo | NR | Both arms | Both arms | Multiple countries |
| McClung, 2006(67) | Postmenopausal women aged ≤80 years with osteopenia or osteoporosis | Osteoporosis and osteopenia | 63 | 85% white 11% hispanic 3% black | 365 | denosumab every 3 months (6, 14 or 30 mg) or every 6 months (14, 60, 100 or 210 mg) vs. placebo | 12 months | Both arms | Both arms | USA |
| McClung, 2009(68) | Ambulatory postmenopausal women aged 45-60 years | Osteopenia | 53.5 | NR | 160 | ibandronate 150 mg/month vs. placebo | 12 months | Both arms | Both arms | USA |
| Meunier, 2004/2009(69, 70) | Postmenopausal women aged ≥50 years with at least 1 vertebral fracture and a lumbar lumbar BMD ≤0.84 g/cm2 | Osteoporosis | 69.3 | 100% white | 1649 | strontium ranelate 2 g/day vs. placebo | 48 months | Both arms | Both arms | Multiple countries |
| Miller, 2008(71) | Ambulatory postmenopausal women with osteoporosis | Osteoporosis | 65.6 | 82% white | 1760 | alendronate 70 mg/week vs. ibandronate 150 mg/month | 12 months | Both arms | Both arms | Multiple countries |
| Miller, 2016a(72) | Postmenopausal ambulatory women aged ≥50 years who received oral bisphosphonate therapy for ≥2 years | Osteoporosis | 69 | 96.9% white, 1.4% asian, 0.2% black or african american, 1.6% other | 643 | denosumab sc 60 mg single dose + iv placebo vs. zoledronate iv 5 mg single dose + sc placebo | 12 months | Both arms | Both arms | Multiple countries |
| Miller, 2016b(73) | Postmenopausal women aged 49-86 years | Osteoporosis | 68.8 | 79.7% white, 16.1% asian, 3% black or african american, 1.3% other | 2463 | teriparatide 20 µg//day vs. abaloparatide 80 µg/day vs. placebo | 18 months | Both arms | Both arms | Multiple countries |
| Morii, 2003(74) | Postmenopausal women aged ≤80 years with osteoporosis | Osteoporosis | 64.7 | 100% asian | 202 | raloxifene 60 or 120 mg / day vs. placebo | 12 months | Both arms | Both arms | Japan |
| Mortensen, 1998(75) | Postmenopausal women for 6-60 months with normal BMD | Normal BMD | 51.6 | 100% white | 111 | risedronate 5 mg/day or 5 mg/day the first two week each month vs. placebo | 24 months | Both arms | Both arms | USA and Denmark |
| Mosekilde, 2000(76) | Women aged 45-58 years with intact uterus and 3 to 24 months from last menstruation with perimenopausal symptoms | Normal BMD | 49.8 | NR | 1006 | HRT (oestradiol 2 mg/day [day 1-12], norethisterone acetate 1 mg/day [day 13-22], oestradiol 1 mg/day [day 23-28]) vs. placebo | 60 months | No | No | Denamark |
| Muscoso, 2004(77) | Postmenopausal women with osteoporosis | Osteoporosis | 68 | NR | 1200 | alendronate 10 mg/day vs. risedronate 5 mg/day vs. raloxifene 60 mg/day | 24 months | Both arms | Both arms | Italy |
| Nachtigall, 1979(78) | Postmenopausal women | NR | 55 | NR | 168 | HRT (conjugated estrogen 2.5 mg/day + MPA 10 mg/day) vs. placebo | 120 months | No | No | USA |
| Nakamura, 2012a(79) | Ambulatory postmenopausal women aged ≤80 years | Osteoporosis | 65.1 | 100% asian | 212 | denosumab 14, 60, 100 mg/6 months vs. placebo | 12 months | Both arms | Both arms | Japan |
| Nakamura, 2012b(80) | Healthy postmenopausal women aged 65-95 years with 1-5 vertebral fractures with low BMD | Osteoporosis | 75.3 | 100% asian | 549 | teriparatide sc 56.5 µg/week vs. placebo | 18 months | Both arms | Both arms | Japan |
| Nakamura, 2014(81) | Postmenopausal women aged ≥50 years with 1 to 4 prevalent vertebral fractures | Osteoporosis | 69.5 | 100% asian | 898 | denosumab 60 mg/6 months vs. placebo | 24 months | Both arms | Both arms | Japan |
| Neer, 2001(82) | Ambulatory postmenopausal women for at least 5 years with osteoporosis | Osteoporosis | 70 | 98% white | 1637 | teriparatide 20 or 40 µg/day vs. placebo | 18 months | Both arms | Both arms | Multiple countries |
| Overgaard, 1992(83) | Healthy women aged 68-72 years with bone mineral content on average 30% below the mean value for healthy premenopausal women (distal forearm) | Osteoporosis | 68-72 | NR | 308 | calcitonin (salmon calcitonin) intranasal 50, 100, or 200 IU/day vs. placebo | 24 months | Both arms | No | Denmark |
| Panico, 2011(84) | Postmenopausal women with back pain, osteoporosis, and 2 vertebral fractures | Osteoporosis | 62.6 | NR | 81 | alendronate 70 mg/week vs. teriparatide 20 µg/day | 18 months | Both arms | Both arms | Italy |
| Pfeifer, 2000(85) | Ambulatory healthy women aged ≥70 years with 25-hydroxycholecalciferol serum level below 50 nmol/l | NR | 74.8 | NR | 148 | vitamin D 800 IU/day vs. control | 12 months | Both arms | No | Germany |
| Pols, 1999(86) | Postmenopausal women for 3 years aged 85 years with osteoporosis. | Osteoporosis and osteopenia | 62.8 | 94% white | 1908 | alendronate 10 mg/day vs. placebo | 12 months | Both arms | No | Multiple countries |
| Porthouse, 2005(87) | Postmenopausal women aged ≥70 years with risk factor for hip fracture | NR | 76.8 | NR | 3314 | calcium carbonate 1 g/day + vitamin D3 1600 IU/day vs. control | 18 months | No | No | UK |
| Prince, 2006(88) | Postmenopausal women ≥70 years | Osteoporosis | 75.2 | NR | 1460 | calcium carbonate 1.2 g/day vs. placebo | 60 months | No | NR | Australia |
| Radford, 2014(89) | Healthy postmenopausal women | Normal BMD | 74.1 | NR | 1471 | calcium 1 g/day vs. placebo | 60 months | No | No | New Zealand |
| Recker, 1999(90) | Healthy white women aged >65 years and spinal BMD 0.9 g/cm2 or less | Osteopenia or Osteoporosis | 73 | 100% white | 128 | HRT (CEE 0.3 mg/day + MPA 2.5 mg/day) vs. placebo | 42 months | Both arms | Both arms | USA |
| Recker, 2004(91) | Postmenopausal women with BMD T score -2 to -5 and one to four prevalent vertebral fractures | Osteoporosis | 67 | NR | 2862 | ibandronate 0.5 or 1 mg/3 months vs. placebo | 36 months | Both arms | Both arms | NR |
| Recker, 2007(92) | Ambulatory postmenopausal women aged 50-80 years | Osteoporosis | 65.6 | 87% white | 1423 | alendronate 10 mg/day vs. raloxifene 60 mg/day | 10.8 months | Both arms | Both arms | USA |
| Recknor , 2013(93) | Postmenopausal women with low bone density treated previously with oral biphosphonate therapy | Osteopenia and Osteoporosis | 67.2 | 85.5% white | 833 | denosumab 60 mg/6 months vs. ibandronate 150 mg/month | 12 months | Both arms | Both arms | Multiple countries |
| Reginster, 2000(94) | Ambulatory women aged ≤85 years with ≥2 vertebral fracture | Osteoporosis | 71 | NR | 814 | risedronate 5 mg/day vs. placebo | 36 months | Both arms | Those with low Vit. D | Multiple countries |
| Reginster, 2005/2008(95, 96) | Ambulatory postmenopausal women aged ≥74 years with osteoporosis | Osteoporosis | 76.47 | NR | 5091 | strontium ranelate 2g/day vs. placebo | 36 and 60 months | Both arms | Both arms | Multiple countries |
| Reid, 2002(97) | Postmenopausal women aged 45-80 years | Osteoporosis and osteopenia | 64 | 99.4% white | 351 | zoledronate, 0.25, 0.5, or 1mg every three months; or 2 mg infusion twice; or one 4mg infusion vs. placebo | 12 months | Both arms | No | Multiple countries |
| Reid, 2004(98) | Postmenopausal women aged 40-60 | Normal BMD or Osteopenia | 53 | 95% white | 461 | raloxifene 60 or 150 mg/day vs. placebo | 36 months | Both arms | NR | Multiple countries |
| Rico, 1995(99) | Postmenopausal women with osteoporosis | Osteoporosis | 69.2 | NR | 72 | calcitonin (salmon calcitonin) im 100 IU/day vs. control | 24 months | Both arms | No | Spain |
| Rogers, 2009(100) | Women aged >50 years with menopause for >5 years with BMD T-score between -1 to -2.5 | Osteopenia | 63.4 | NR | 51 | lasofoxifene 0.25 mg/day vs. placebo | 24 months | Both arms | Both arms | UK |
| Saag, 2017 (101) | Ambulatory postmenopausal women 55 to 90 years | Osteoporosis | 74 | 32% hispanic | 4093 | Monthly sc romosozumab (210 mg) vs. weekly oral alendronate | 12 months | Both arms | Both arms | Multiple countries |
| Salovaara, 2010(102) | Women aged ≥65 years | NR | 67.4 | NR | 3195 | vitamin D (cholecalciferol) 800 IU/day + calcium carbonate 1 g/day vs. control group | 36 months | Optional | Optional | Finland |
| Silverman, 2008/2012(103, 104) | Healthy postmenopausal women aged 55-85 with osteoporosis. At least 2 years of menopause | Osteoporosis | 66.4 | 87% white | 7492 | bazedoxifene 20 or 40 mg/day vs. raloxifene 60 mg/day vs. placebo | 36 months for raloxifene arm, 60 months for the rest. | Both arms | Both arms | Multiple countries |
| Tanko, 2004(105) | Healthy postmenopausal women aged 55-85. At least 5 years of menopause | Normal BMD | 55-85 | 100% white | 277 | calcitonin (salmon calcitonin) oral 0.15, 0.4, 1, or 2.5 mg/day or 1 mg/interdaily vs. placebo | 36 months | Both arms | Both arms | Denmark and Belgium |
| Tierney, 2009(106) | Women aged ≥60 years with last menstrual cycle ≥12 months before | NR | 74.7 | 93% white, 4.2% black, 2.8% asian | 142 | HRT (17β-estradiol micronized 1 mg/day + norethindrone 0.35 mg/3 days per week) vs. placebo | 24 months | NR | NR | Canada |
| Ushiroyama, 2001(107) | Postmenopausal Japanese women for at least 6 months with osteopenia or osteoporosis | Osteopenia and osteoporosis | 52.5 | NR | 151 | calcitonin im 10 IU twice a month vs. vitamin D (1ɑ-hydroxycholecalciferol) 1 µg/day vs. control | 24 months | No | No | Japan |
| Vickers, 2007(108) | Postmenopausal (no menstrual period for 12 months) women aged 50-69 years | NR | 62.8 | NR | 6026 | HRT (estrogen 0.625 mg/ day or estrogen 2.5 mg/day + Progesterone 5 mg/day) vs. placebo | 11.9 months | No | No | Japan |
| Weiss, 1999(109) | Postmenopausal women aged ≥45 years, who had undergone hyesterectomy without oophorectomies | NR | 51.2 | 83.4% white, 6.9% black, 5.1% hispanic | 175 | HRT (17β-E2 transdermal system of 0.025,0.05,0.06, and 0.1 mg/day) vs. placebo | 24 months | Both arms | No | USA |
| Wimalawansa, 1998(110) | Postmenopausal white women with osteoporosis | Osteoporosis | 64.9 | 100% white | 36 | HRT (premarin 0.625 mg/day + norgestrel 150 µg for 12 days each month) vs. control | 48 months | Both arms | Both arms | NR |
| Yan, 2009(111) | Ambulatory postmenopausal women with osteoporosis aged ≤85 years | Osteoporosis | 65 | 100% asian | 560 | alendronate 70 mg/week vs. placebo | 12 months | Both arms | Both arms | China |

# Supplemental table 2. Risk of Bias Assessment

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author, year** | **Lost follow-up** | **Length of follow-up (mo)** | **Baseline imbalance** | **Allocation concealment** | **Blinding** | | | | | **Funding** | **Fracture assessment** | **Overall RoB** |
| **CG** | **OA** | **DC** | **DA** | **P** |
| Alexandersen, 1999(1) | 28% | 22 | No | Probably Yes | Yes | Yes | NR | NR | Yes | Not reported or unclear | Medical records or radiologic reports | Low |
| Bai, 2013(2) | 0% | 24 | No | NR or unclear | NR | NR | NR | NR | NR | Only not for profit source | Documented by medical personnel | High |
| Bischoff,2003(3) | 27% | 3 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit and non-for –profit sources | NR | High |
| Black, 1996(4) | 4% | 36 | No | Probably Yes | Yes | NR | NR | NR | Yes | Not reported or unclear | Medical records or radiologic reports | Low |
| Black, 2007(5) | NR | 36 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Blair, 2009(6) | NR | 6 | NR | Probably No | NR | NR | NR | NR | NR | Includes for-profit source | Documented by medical personnel | High |
| Bock, 2012(7) | 2% | 12 | No | Probably Yes | Yes | NR | NR | NR | Yes | Only not-for-profit source. | Documented by medical personnel | Low |
| Body, 2002(8) | 0.50% | 14 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| Bolton-Smith, 2007(9) | 13.80% | 24 | No | Probably Yes | Yes | NR | NR | NR | Yes | Only not-for-profit source. | NR | Low |
| Bone, 1997(10) | NR | 24 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| Bone, 2008(11) | 14% | 24 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| Bush, 1996(12) | 27.10% | 36 | No | NR or unclear | Yes | NR | NR | NR | Yes | Only not-for-profit source | NR | High |
| Cauley, 2003(13) | NR | 18 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | By semiannual questionnaire | High |
| Chapuy, 1992/1994(14, 15) | 46% | 18 | No | NR or unclear | NR | NR | NR | NR | Yes | Only not-for-profit source. | Medical records or radiologic reports | High |
| Chapuy, 2002(16) | 4.40% | 24 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Medical records or radiologic reports | High |
| Chesnut, 2000(17) | 59.30% | 60 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | Medical records or radiologic reports | Low |
| Chesnut, 2004(18) | NR | 36 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Clemmesen, 1997(19) | 27% | 36 | No | Probably No | Yes | Yes | NR | NR | Yes | Not reported or unclear | Documented by medical personnel | High |
| Cosman, 2009(20) | 15.60% | 18 | No | Probably Yes | No | NR | NR | NR | No | Includes for-profit source | NR | Unclear |
| Cosman, 2011(21) | 0% | 12 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for- profit source | Documented by medical personnel | Low |
| Cosman, 2016(22) | 0.6% | 12 | No | Probably Yes | Yes | No | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Cummings, 1998(23) | 4% | 50.4 | No | Probably Yes | Yes | Yes | Yes | Yes | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Cummings, 2008(24) | 9.90% | 34 | No | Probably No | Yes | NR | Yes | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| Cummings, 2009(25) | NR | 36 | No | NR or unclear | NR | NR | NR | NR | NR | Includes for-profit source | Medical records or radiologic reports | High |
| Cummings, 2010(26) | NR | 60 | No | Probably No | NR | NR | NR | NR | NR | Not reported or unclear | Vertebral fractures by medical personnel, non-vertebral by self report | High |
| Dursun, 2001(27) | NR | 12 | No | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | Lateral and anteroposterior X-rays for vertebral fractures | High |
| Ensrud, 2008(28) | NR | 67.2 | No | Probably Yes | Yes | Yes | Yes | Yes | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Ettinger, 1999(29) | NR | 36 | No | Probably Yes | Yes | Yes | NR | NR | Yes | Includes for-profit source | Vertebral fractures by medical personnel, non-vertebral not specified | Low |
| Fogelman, 2000(30) | 34% | 24 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| Fogelman, 2008(31) | NR | 18 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Vertebral fractures by medical personnel, non-vertebral by self report | High |
| Gallagher, 2001(32) | 14.40% | 36 | Yes, increased vertebral fractures in Vitamin D arm | Probably No | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| Garay Lillo, 1997(33) | 43.70% | 24 | NR | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | NR | High |
| Gennari, 1985(34) | 45.10% | 12 | No | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | Documented by medical personnel | High |
| Greenspan, 1998(35) | 25% | 30 | Yes, the mean intertrochanteric BMD was slightly higher in the placebo group than in the alendronate group | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | High |
| Greenspan, 2002(36) | NR | 24 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | Low |
| Greenspan, 2007(37) | 0% | 18 | No | Probably Yes | Yes | Yes | NR | NR | NR | Includes for-profit source | Documented by medical personnel | Unclear |
| Greenspan, 2015(38) | 7.2% | 24 | No | NR or unclear | Yes | Yes | Yes | Yes | Yes | Only not-for-profit source | Documented by medical personnel | High |
| Grey, 2009(39) | 2% | 24 | No | Probably Yes | Yes | Yes | Yes | NR | Yes | Only not-for-profit source | NR | Low |
| Grey, 2014(40) | 7% | 24 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes For profit source | NR | Low |
| Gruber, 1984(41) | 11.10% | 24 | Yes, treatment group had less years with menopause and more number of vertebral fractures | Probably No | NR | NR | NR | NR | NR | Includes For profit source | Documented by medical personnel | High |
| Hadji, 2012(42) | 25.60% | 18 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source. | Documented by medical personnel | High |
| Harris, 1999(43) | 2.10% | 36 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Harwood, 2004(44) | 31.30% | 12 | No | Probably Yes | NR | NR | NR | NR | NR | Not reported or unclear | NR | Unclear |
| Henriksen, 2016(45) | 10.1% | 36 | No | Probably Yes | Yes | Yes | Yes | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Hizmetli, 1998(46) | 24.30% | 24 | No | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | Documented by medical personnel | High |
| Hooper, 2005(47) | 22.20% | 24 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Hulley, 1998(48) | 5.60% | 49 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | Low |
| Ishida, 2004(49) | 6.40% | 24 | No | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | Documented by medical personnel | High |
| Itabashi, 2011(50) | 0.47% | 24 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Vertebral fractures by medical personnel, non-vertebral by self report | High |
| Iwamoto, 2008(51) | 16.30% | 12 | No | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | Documented by medical personnel | High |
| Iwamoto, 2011(52) | 0% | 6 | Yes, women in the Calcitonin group were significantly older and thinner. | NR or unclear | Yes | NR | NR | NR | NR | Only not for profit source | Documented by medical personnel | High |
| Jackson, 2006(53) | 7% | 24 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| Jacobsen, 2012(54) | 59.8% (79% dropped from the Tibolone arm due to the results of the Long-Term Intervention on Fractures with Tibolone study (higher risk of CVAs) | 24 | No | Probably Yes | Yes | NR | NR | NR | Yes | Only not for profit source | NR | Low |
| Koh, 2016(55) | 4.4% | 6 | No | NR or unclear | Yes | Yes | Yes | NR | Yes | Includes for-profit source | Documented by medical personnel | Unclear |
| Komulainen, 1998(56) | 5% | 60 | No | Probably Yes | NR | NR | NR | NR | NR | Not reported or unclear | Documented by medical personnel | Unclear |
| Lees, 2001(57) | 38.20% | 24 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | Low |
| Liberman, 1995(58) | NR | 36 | No | NR or unclear | Yes | Yes | NR | NR | Yes | Includes for-profit source | Vertebral fractures by medical personnel, non-vertebral not specified | High |
| Lindsay, 1990(59) | 20% | 24 | No | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | NR | High |
| Luckey, 2004(60) | 18.40% | 12 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | Low |
| Lufkin, 1992(61) | 9.30% | 12 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| Lufkin, 1998(62) | NR | 12 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | Vertebral fractures by medical personnel, non-vertebral not specified | Low |
| Macdonald, 2013(63) | >30% | 12 | No | NR or unclear | Yes | NR | NR | NR | Yes | Only not for profit source | Documented by Self report | High |
| McClung, 2001(64) | NR | 28 | No | NR or unclear | NR | NR | NR | NR | NR | Includes for-profit source | Documented by medical personnel | High |
| McClung, 2004(65) | 28.70% | 72 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | High |
| McClung, 2005(66) | NR | 18 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| McClung, 2006(67) | NR | 12 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | Low |
| McClung, 2009(68) | NR | 12 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Vertebral fractures by medical personnel, non-vertebral by self report | High |
| Meunier, 2004/2009(69, 70) | 12.6%/20.5% | 36/48 | No | Probably No | Yes | NR | NR | NR | Yes | Only not-for-profit source/Not reported or unclear | Documented by medical personnel/Vertebral fractures by radiographs. non-vertebral fractures by radiographs and medical reports | High |
| Miller, 2008(71) | 12% | 12 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | High |
| Miller, 2016a(72) | 0.0% | 6 | No | NR or unclear | Yes | Yes | Yes | Yes | Yes | Includes for-profit source | Documented by medical personnel | Unclear |
| Miller, 2016b(73) | 22.8% | 18 | No | Probably Yes | No | Yes | Yes | NR | No | Includes for-profit source | Documented by medical personnel | High |
| Morii, 2003(74) | NR | 12 | Yes, Placebo had lower lumbar spine BMD; P = 0.004 | Probably Yes | Yes | Yes | NR | NR | Yes | Includes for-profit source | Vertebral fractures by medical personnel, non-vertebral not specified | Low |
| Mortensen, 1998(75) | NR | 36 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| Mosekilde, 2000(76) | 10.80% | 60 | No | Probably Yes | NR | NR | NR | NR | NR | Only not-for-profit source | Documented by medical personnel | Unclear |
| Muscoso, 2004(77) | NR | 24 | No | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | NR | High |
| Nachtigall, 1979(78) | NR | 120 | NR | Probably No | Yes | NR | NR | NR | Yes | Not reported or unclear | NR | High |
| Nakamura, 2012a(79) | 8% | 12 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source. | Documented by medical personnel | Low |
| Nakamura, 2012b(80) | 23.50% | 18 | No | NR or unclear | Yes | Yes | NR | NR | Yes | Includes for-profit source | Medical records or radiologic reports | High |
| Nakamura, 2014(81) | 17.9% | 24 | No | NR or unclear | Yes | Yes | Yes | Yes | Yes | Includes for-profit source | Documented by medical personnel | High |
| Neer, 2001(82) | NR, Base-line and follow-up radiographs available for 81% | 21 | No | NR or unclear | NR | NR | NR | Yes | NR | Includes for-profit source | Documented by medical personnel | High |
| Overgaard, 1992(83) | 15% | 24 | No | Probably Yes | Yes | NR | NR | NR | Yes | Only not-for-profit source | Documented by medical personnel | Low |
| Panico, 2011(84) | 3.70% | 18 | No | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | NR | High |
| Pfeifer, 2000(85) | 7.40% | 12 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Pols, 1999(86) | 11% | 12 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | High |
| Porthouse, 2005(87) | 17.80% | 18 | No | Probably Yes | NR | NR | NR | NR | NR | Includes for-profit source | Documented by medical personnel | Unclear |
| Prince, 2006(88) | 0% | 60 | No | Probably Yes | Yes | Yes | NR | NR | Yes | Only not-for-profit source | Documented by medical personnel | Low |
| Radford, 2014(89) | 10% | 60 | No | Probably Yes | Yes | NR | NR | NR | Yes | Only not for profit source | Documented by Self report | Low |
| Recker, 1999(90) | 16.40% | 42 | No | Probably Yes | Yes | NR | NR | NR | Yes | Only not for profit source | NR | Low |
| Recker, 2004(91) | 1.10% | 36 | No | Probably Yes | Yes | Yes | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Recker, 2007(92) | 1.90% | 10 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Recknor , 2013(93) | 9.50% | 12 | No | Probably Yes | NR | NR | NR | NR | NR | Includes for-profit source | NR | Unclear |
| Reginster, 2000(94) | NR, 58% completed 3 study | 36 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Vertebral fractures by medical personnel, non-vertebral not specified | High |
| Reginster, 2005/2008(95, 96) | 0.03% | 36 and 60 | No | NR or unclear | Yes | NR | NR | NR | Yes | Not reported or unclear | Vertebral fractures by medical personnel, non-vertebral not specified | High |
| Reid, 2002(97) | 10% | 12 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | Vertebral fractures by medical personnel, non-vertebral not specified | High |
| Reid, 2004(98) | 3.9% | 36 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Rico, 1995(99) | 5.6% | 24 | No | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | Documented by medical personnel | High |
| Rogers, 2009(100) | 0.0% | 24 | No | Probably Yes | NR | NR | NR | NR | NR | Includes for-profit source | NR | Unclear |
| Saag, 2017 (101) |  | 12 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Salovaara, 2010(102) | 1.8% | 36 | No | Probably Yes | No | NR | NR | NR | No | Includes for-profit source | Medical records or radiologic reports | Unclear |
| Silverman, 2008/2012(103, 104) | >10% | 36 (Raloxifene arm), 60 (Bazedoxifene and Placebo arm) | No | Probably Yes | Yes | Yes | NR | Yes | Yes | Includes for-profit source | Documented by medical personnel | Low |
| Tanko, 2004(105) | 9.4% | 3 | No | NR or unclear | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | High |
| Tierney, 2009(106) | 9.9% | 24 | No | Probably Yes | Yes | Yes | Yes | Yes | Yes | Only not-for-profit source | NR | Low |
| Ushiroyama, 2001(107) | NR | 24 | No | NR or unclear | NR | NR | NR | NR | NR | Not reported or unclear | NR | High |
| Vickers, 2007(108) | NR | 11.9 | No | Probably Yes | NR | NR | NR | NR | NR | Only not-for-profit source | NR | Low |
| Weiss, 1999(109) | 3.0% | 24 | No | Probably No | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | Unclear |
| Wimalawansa, 1998(110) | 19.4% | 48 | No | Probably Yes | NR | Yes | NR | NR | NR | Not reported or unclear | Documented by medical personnel | Unclear |
| Yan, 2009(111) | 17.0% | 12 | No | Probably Yes | Yes | NR | NR | NR | Yes | Includes for-profit source | NR | Low |

Abbreviations: CG (care giver), OA (outcome assessor), DC (data collector), DA (data analyst), P (patient), NR (not reported)

# Supplemental table 3. Quality of evidence of network estimates (interventions compared to placebo)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Hip** | | | | | | | | | | | | | | | | | | |
| Abaloparatide | Romosozumab | Calcitonin | Lasofoxifene | Strontium ranelate | Tibolone | Hormone therapy | Bazedoxifene | Calcium | Vitamin D + Calcium | Vitamin D | Alendronate | Ibandronate | Risedronate | Zoledronate | Raloxifene | Denosumab | Teriparatide | |
| 0.24 (0.01,4.84) | 0.44 (0.24,0.79) | 0.48 (0.21,1.10) | 0.83 (0.55,1.26) | 0.89 (0.67,1.18) | 0.69 (0.32,1.51) | 0.72 (0.53,0.98) | 0.93 (0.37,2.33) | 1.39 (0.90,2.15) | 0.81 (0.71,0.93) | 0.69 (0.43,1.09) | 0.61 (0.42,0.90) | 0.62 (0.29,1.36) | 0.73 (0.58,0.92) | 0.60 (0.45,0.81) | 0.91 (0.71,1.17) | 0.56 (0.35,0.90) | 0.64 (0.25,1.68) | |
| **L\*\*** | **H** | **L\*†** | **L\*\*** | **L\*\*** | **L\*\*** | **M†** | **L\*\*** | **VL\*\*†** | **M†** | **L\*†** | **H** | **M\*** | **H** | **H** | **M\*** | **H** | **L\*\*** | |
| **Nonvertebral** | | | | | | | | | | | | | | | | | | |
| Abaloparatide | Romosozumab | PTH 1-84 | Calcium | Vitamin D | Lasofoxifene | Calcitonin | Hormone therapy | Tibolone | Bazedoxifene | Vitamin D + Calcium | Strontium ranelate | Alendronate | Ibandronate | Risedronate | Zoledronate | Raloxifene | Denosumab | Teriparatide |
| 0.51 (0.29,0.87) | 0.67 (0.53,0.86) | 0.98 (0.71,1.35) | 0.77 (0.56,1.05) | 0.44 (0.23,0.85) | 0.84 (0.72,0.99) | 0.84 (0.68,1.05) | 0.78 (0.68,0.89) | 0.73 (0.58,0.94) | 0.90 (0.72,1.11) | 0.93 (0.85,1.01) | 0.90 (0.78,1.04) | 0.84 (0.74,0.94) | 1.06 (0.83,1.36) | 0.78 (0.68,0.89) | 0.79 (0.67,0.94) | 0.94 (0.85,1.05) | 0.80 (0.67,0.96) | 0.62 (0.47,0.80) |
| **H** | **H** | **M\*** | **L\*†** | **M†** | **M\*** | **L\*†** | **M†** | **M†** | **M\*** | **L\*†** | **M\*** | **H** | **M\*** | **H** | **H** | **M\*** | **H** | **H** |
| **Vertebral** | | | | | | | | | | | | | | | | | | |
| Abaloparatide | Romosozumab | Vitamin D | PTH 1-84 | Strontium ranelate | Tibolone | Calcitonin | Hormone therapy | Lasofoxifene | Bazedoxifene | Calcium | Vitamin D + Calcium | Alendronate | Ibandronate | Risedronate | Zoledronate | Raloxifene | Denosumab | Teriparatide |
| 0.14 (0.05,0.42) | 0.33 (0.22,0.49) | 0.85 (0.46,1.59) | 0.41 (0.22,0.77) | 0.60 (0.46,0.78) | 0.56 (0.36,0.87) | 0.65 (0.50,0.85) | 0.65 (0.46,0.92) | 0.67 (0.46,0.98) | 0.61 (0.41,0.90) | 0.70 (0.48,1.04) | 0.88 (0.61,1.27) | 0.57 (0.45,0.71) | 0.67 (0.48,0.93) | 0.61 (0.48,0.78) | 0.38 (0.25,0.58) | 0.59 (0.46,0.76) | 0.32 (0.22,0.45) | 0.27 (0.19,0.38) |
| **H** | **H** | **L\*\*** | **H** | **H** | **M†** | **M†** | **M†** | **H** | **H** | **L\*†** | **L\*†** | **H** | **H** | **H** | **H** | **H** | **H** | **H** |

Quality of evidence (also called certainty in evidence) is categorized as: VL: very low, L: low, M: moderate, H: high. The network is judged to have adequate consistency and transitivity. There was no concern about indirectness of fracture outcomes. There was no clear and reliable evidence of publication bias.

\* Serious concern about imprecision

\*\* Very serious concern about imprecision

† Serious concern about risk of bias

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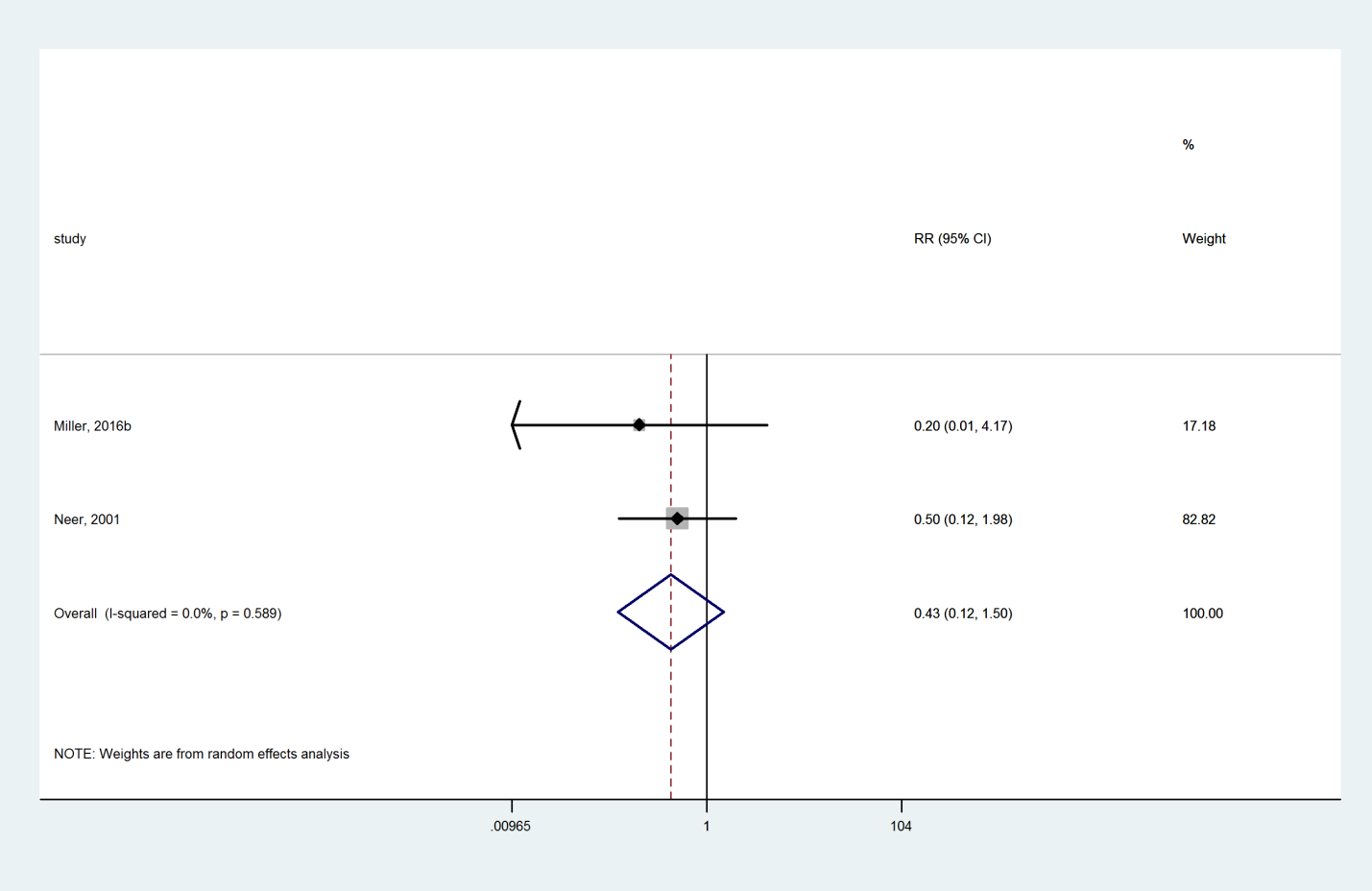
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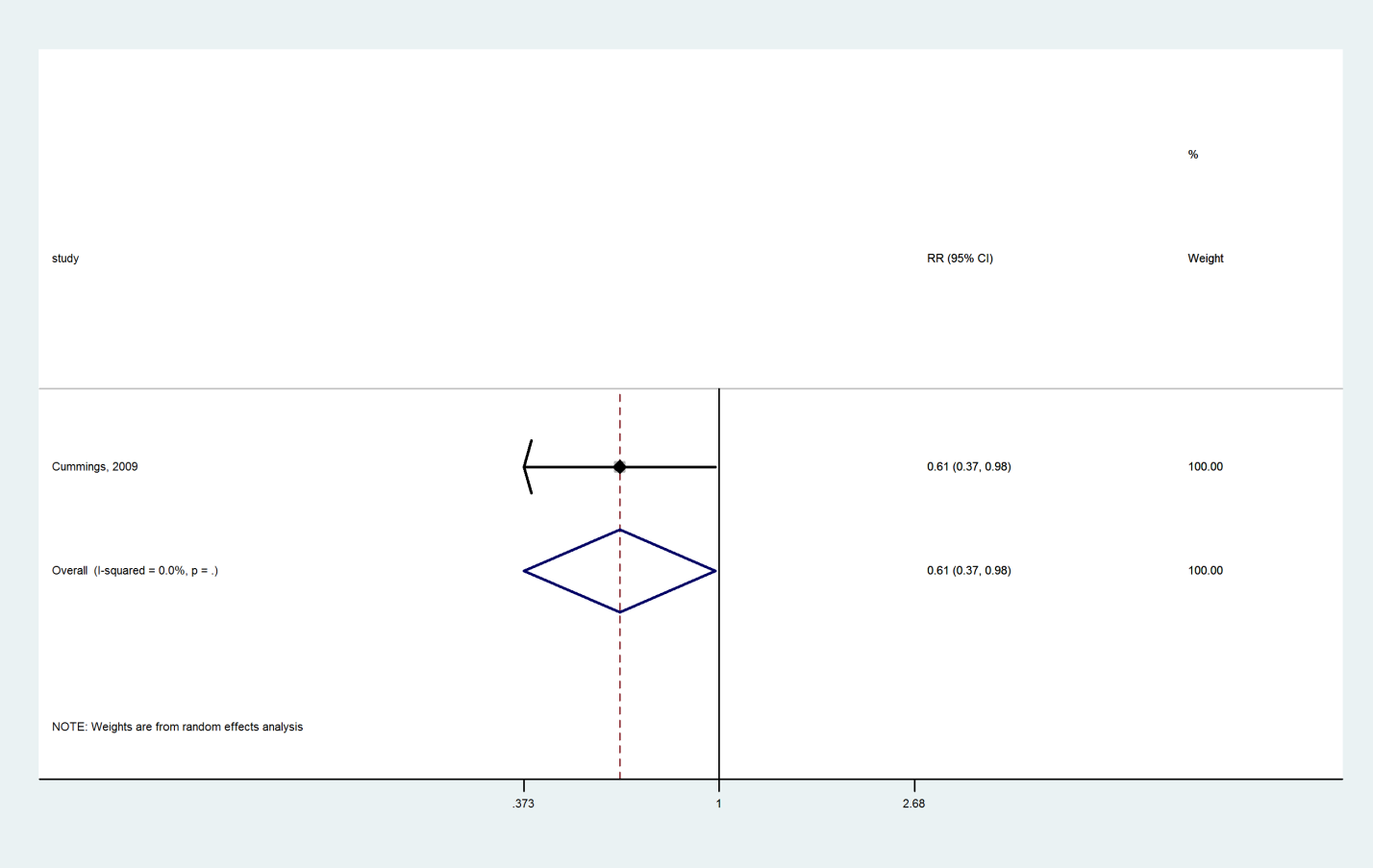
# Direct Comparisons

## Hip fracture

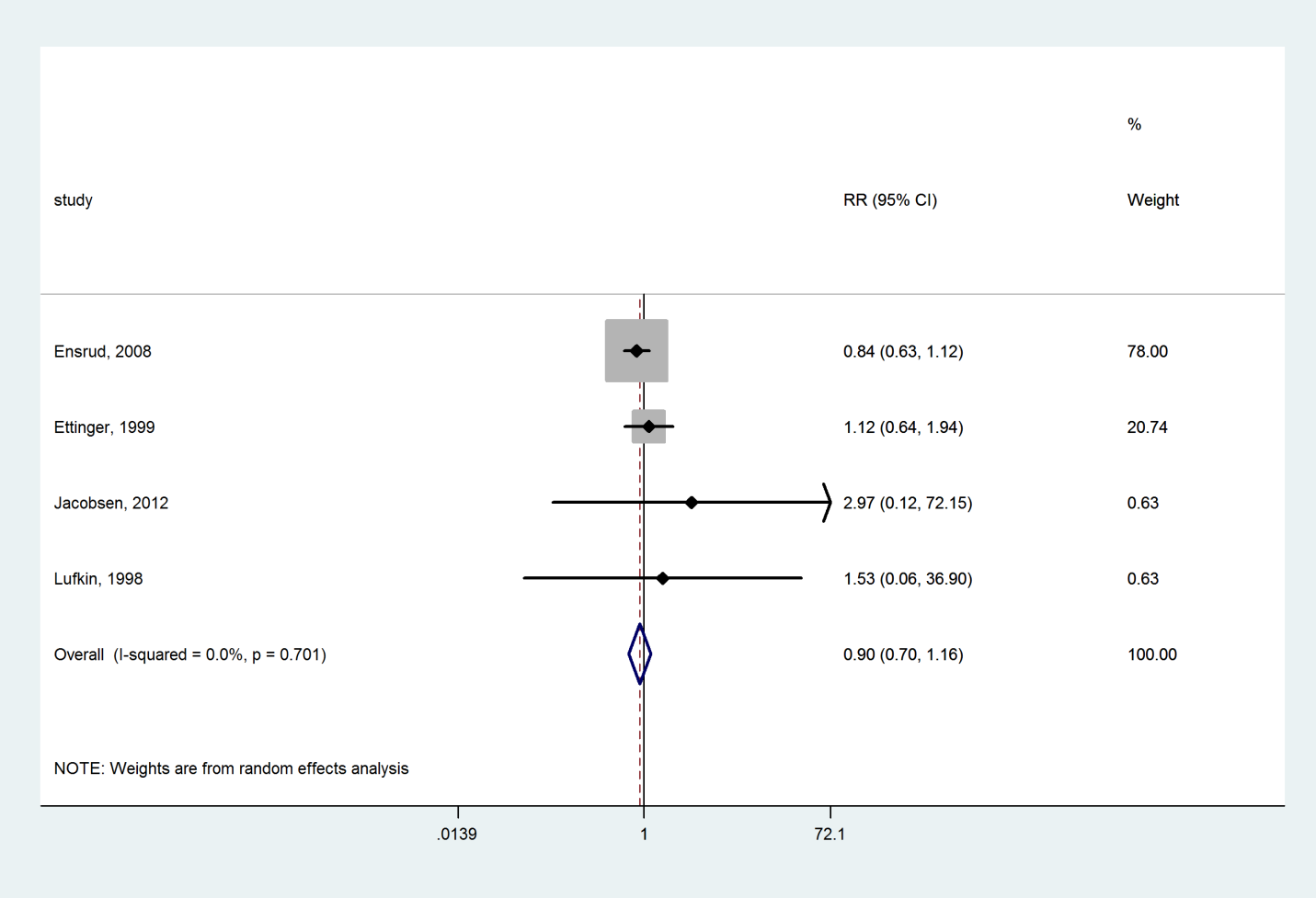
### Teriparatide compared with Placebo



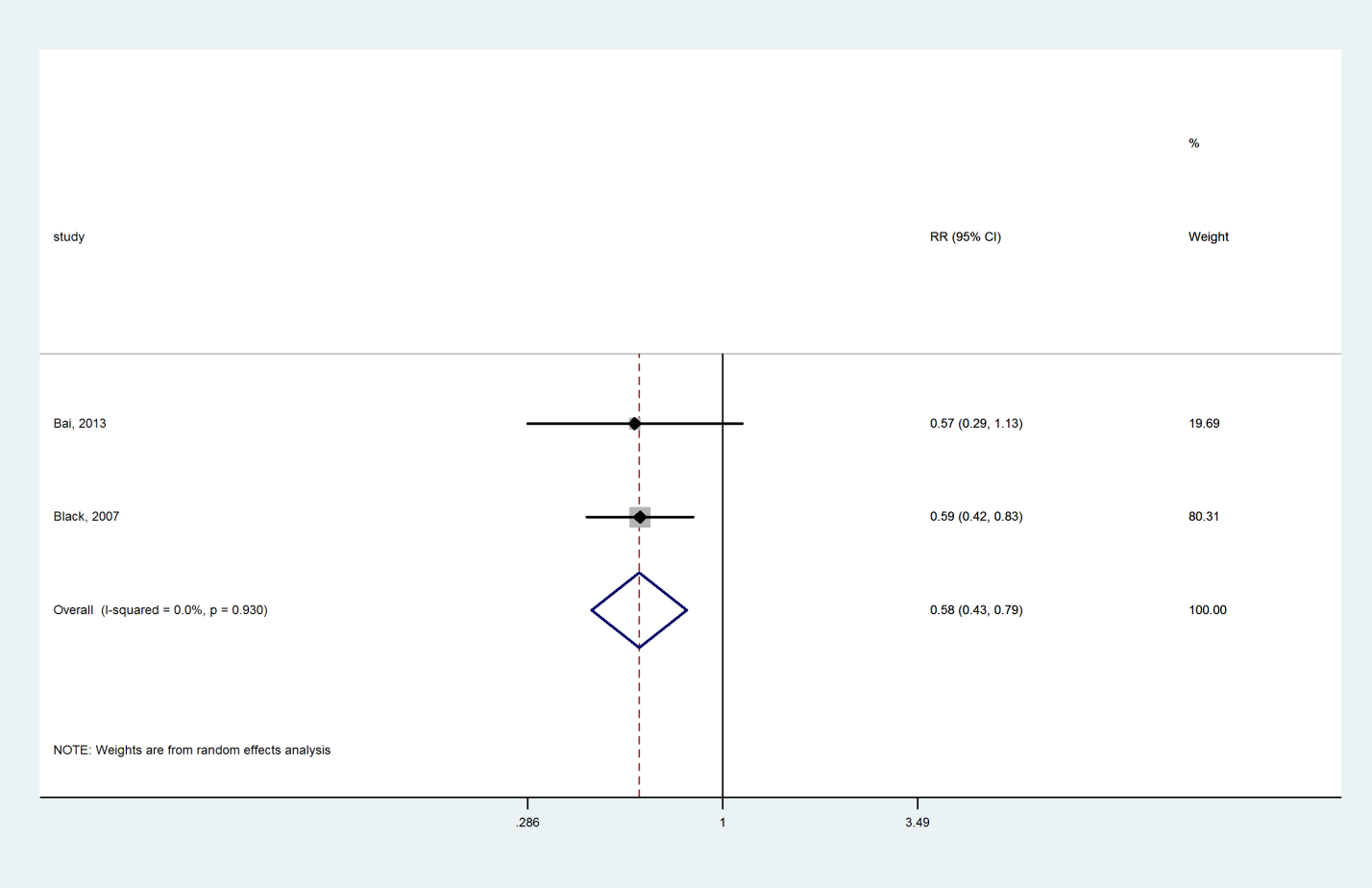
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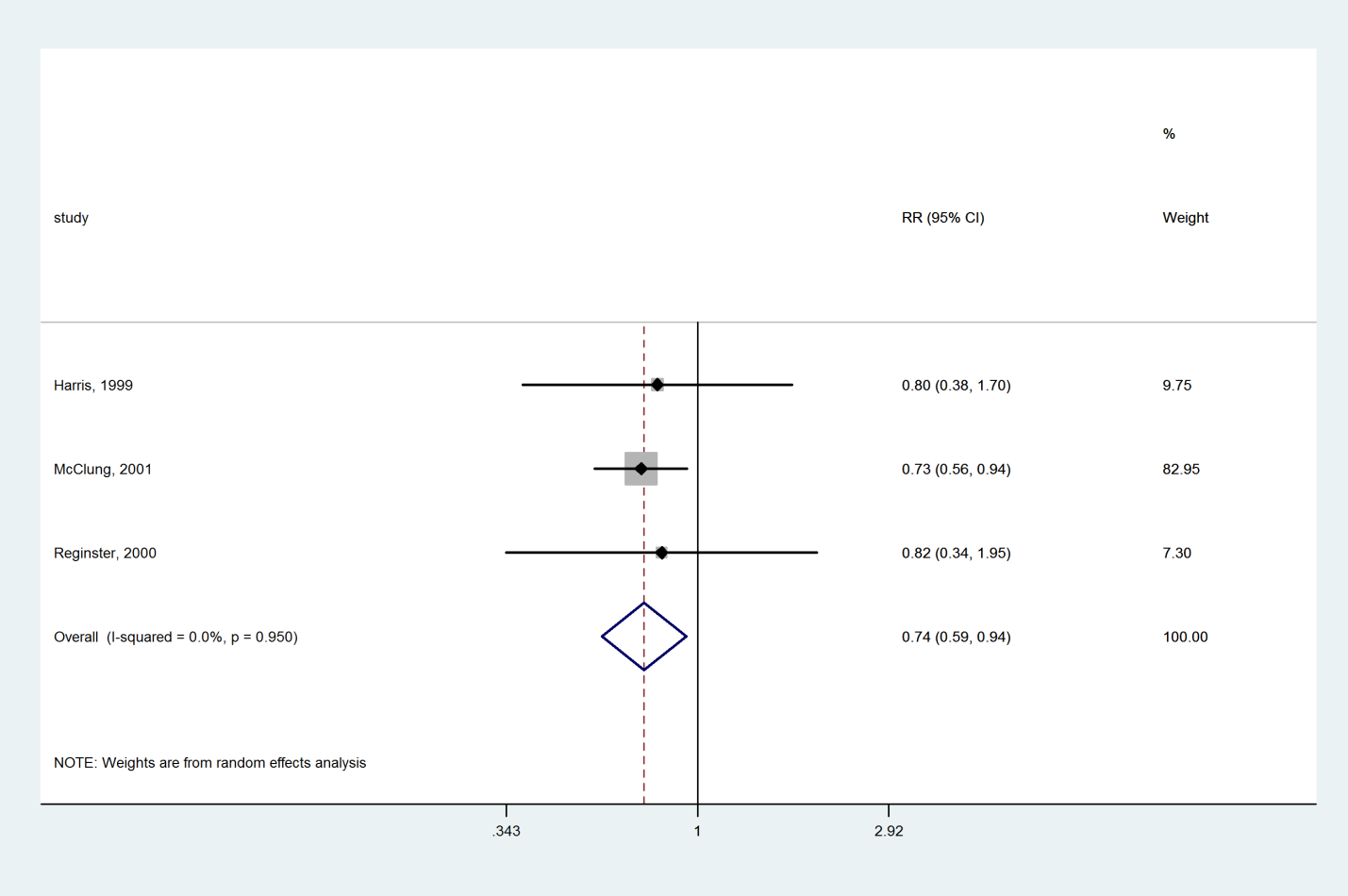
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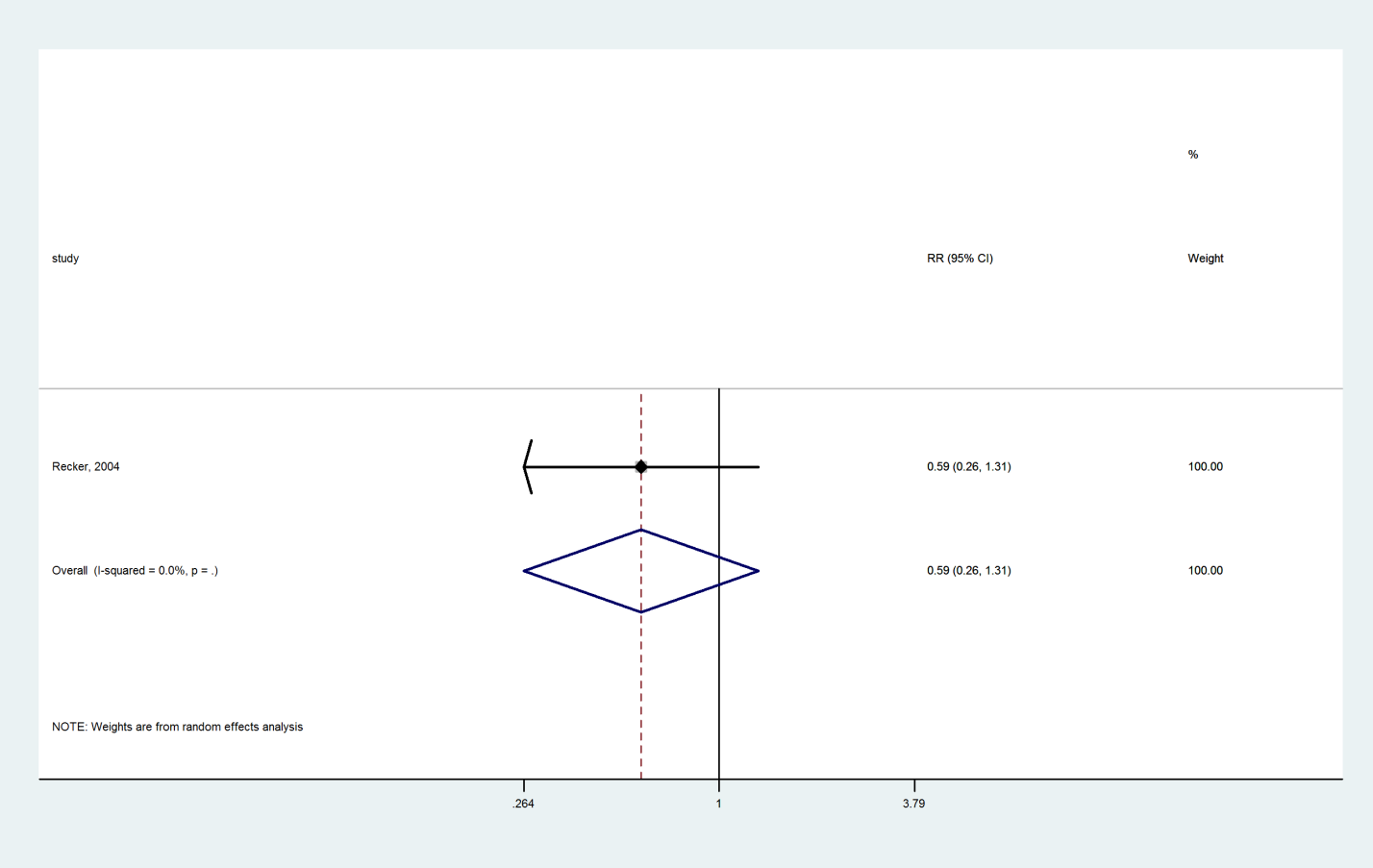
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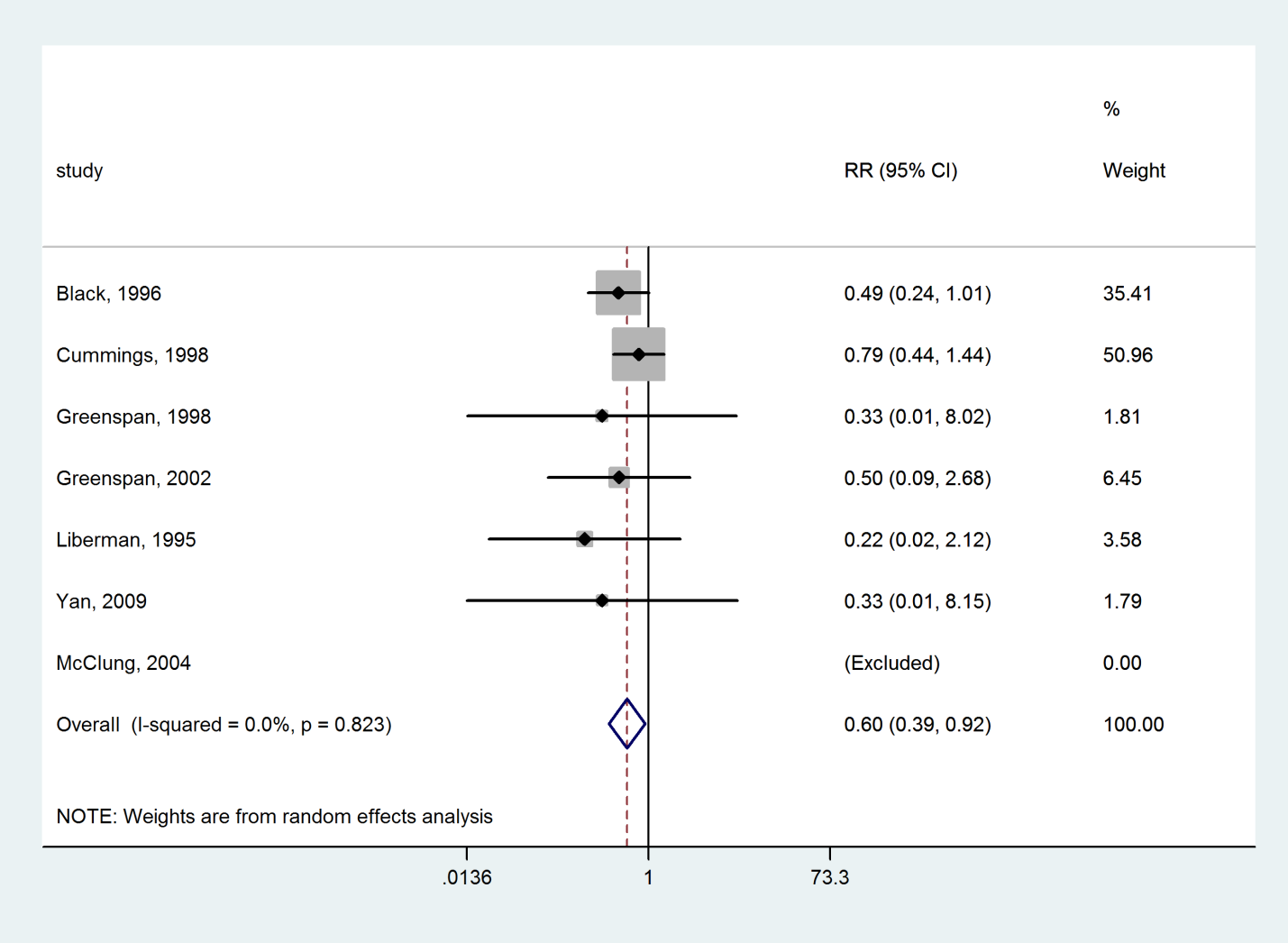
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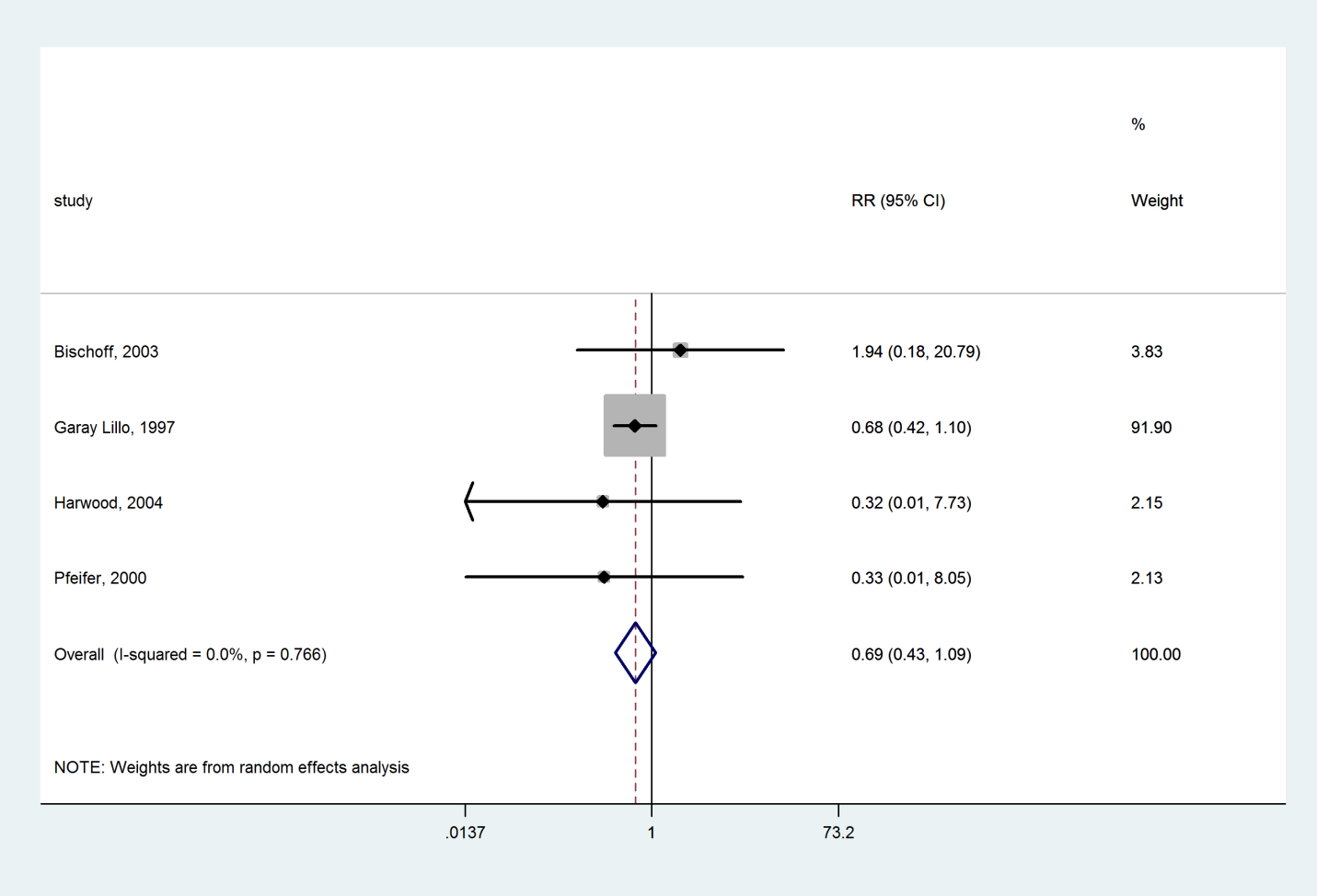
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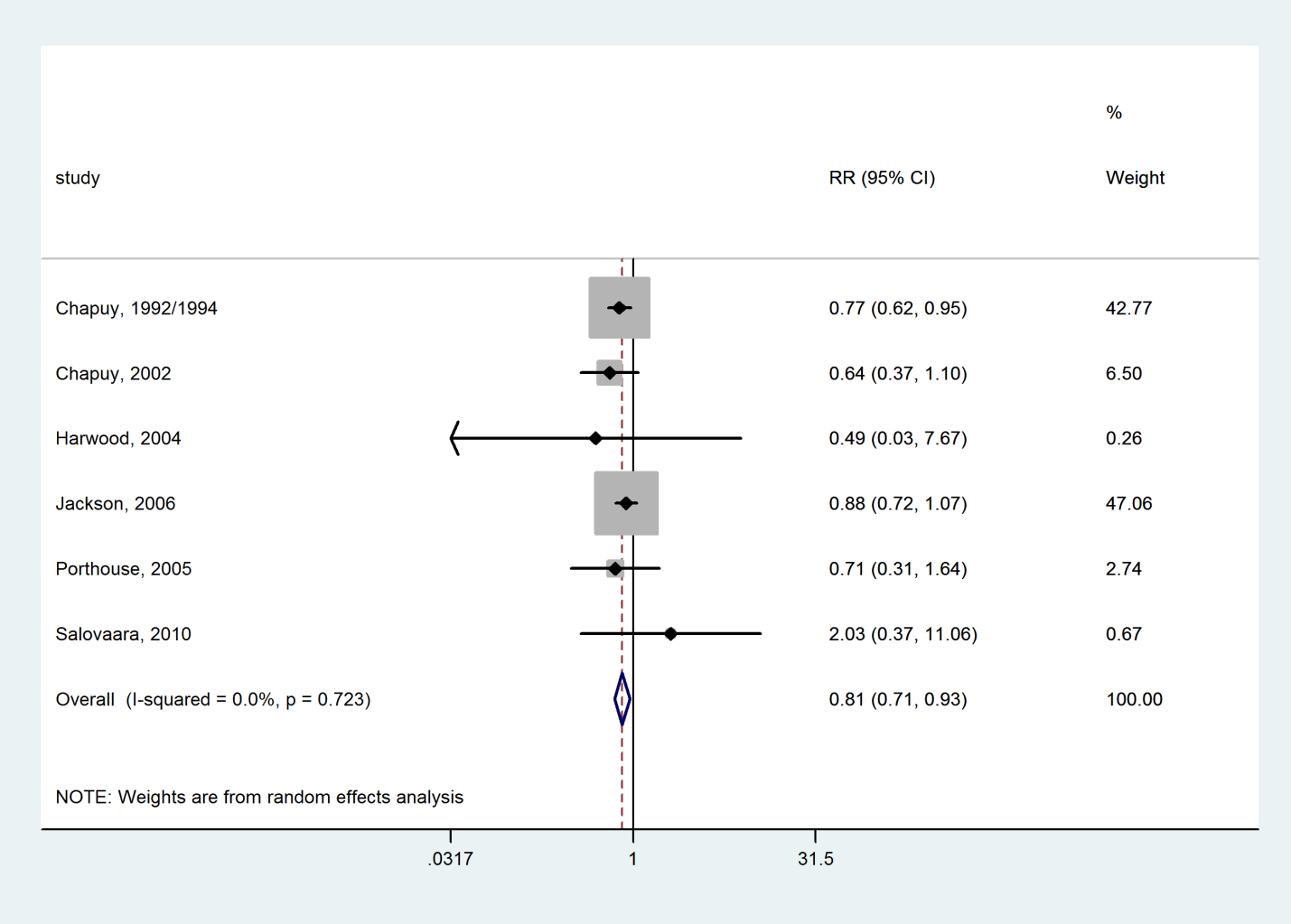
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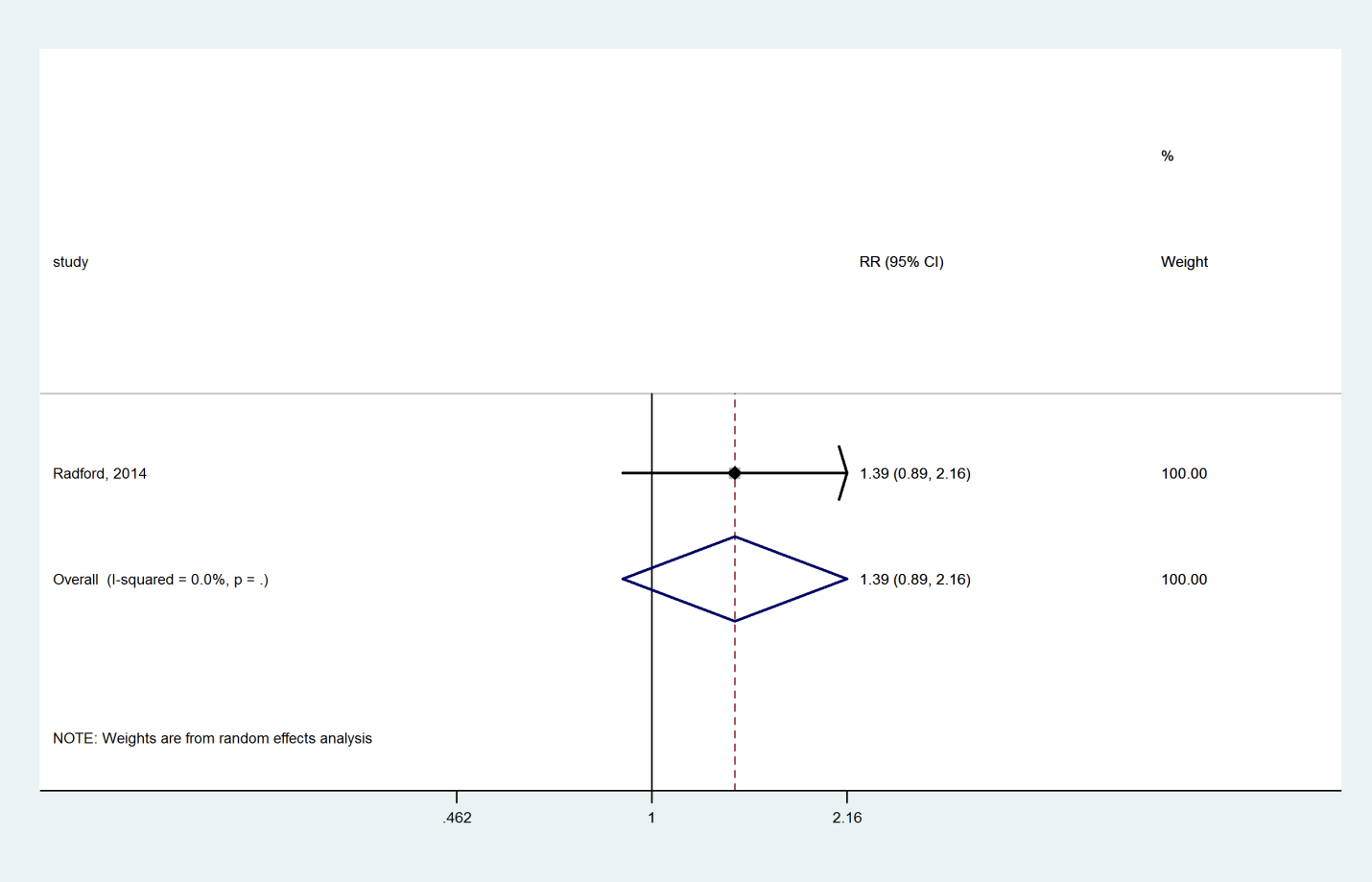
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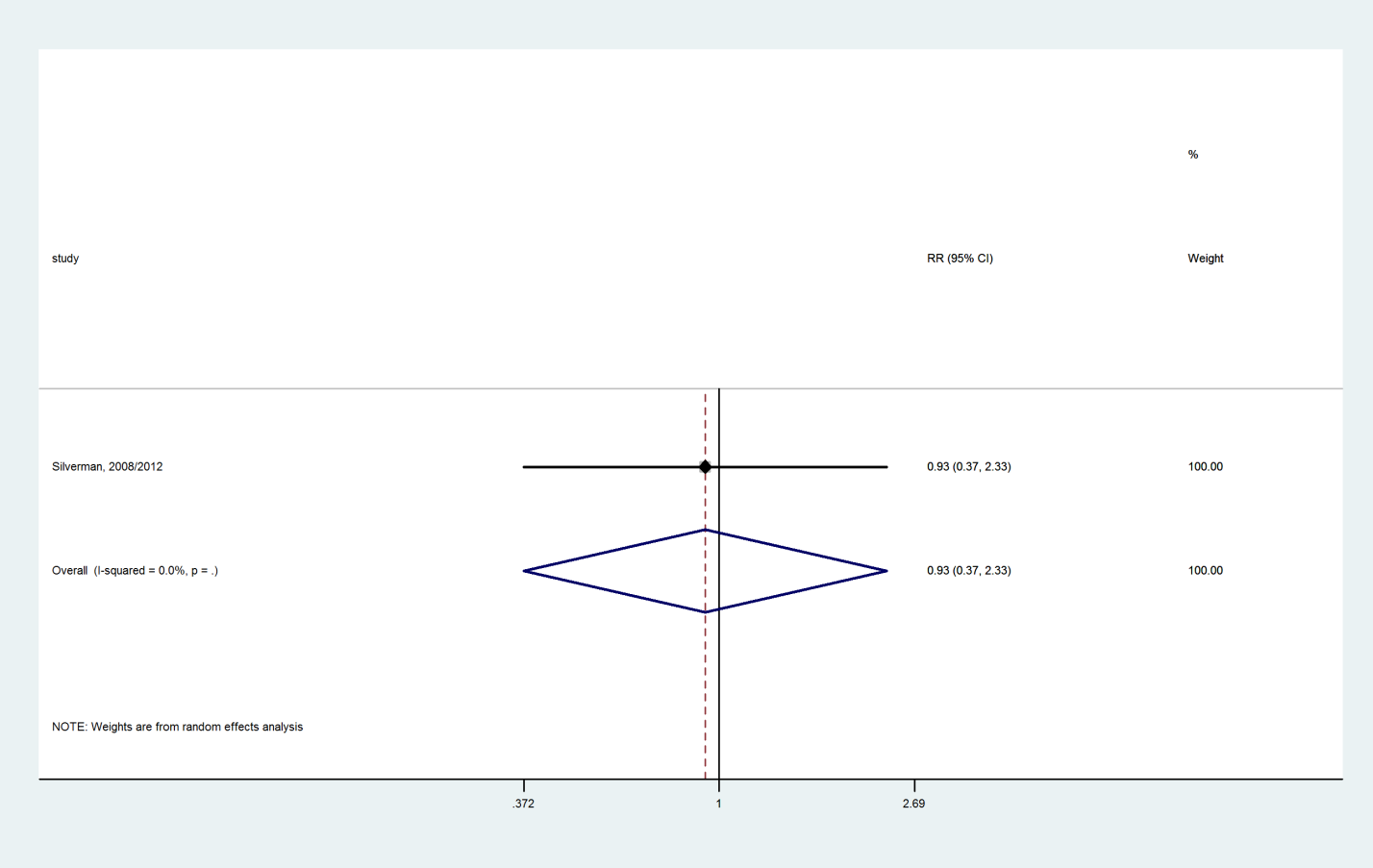
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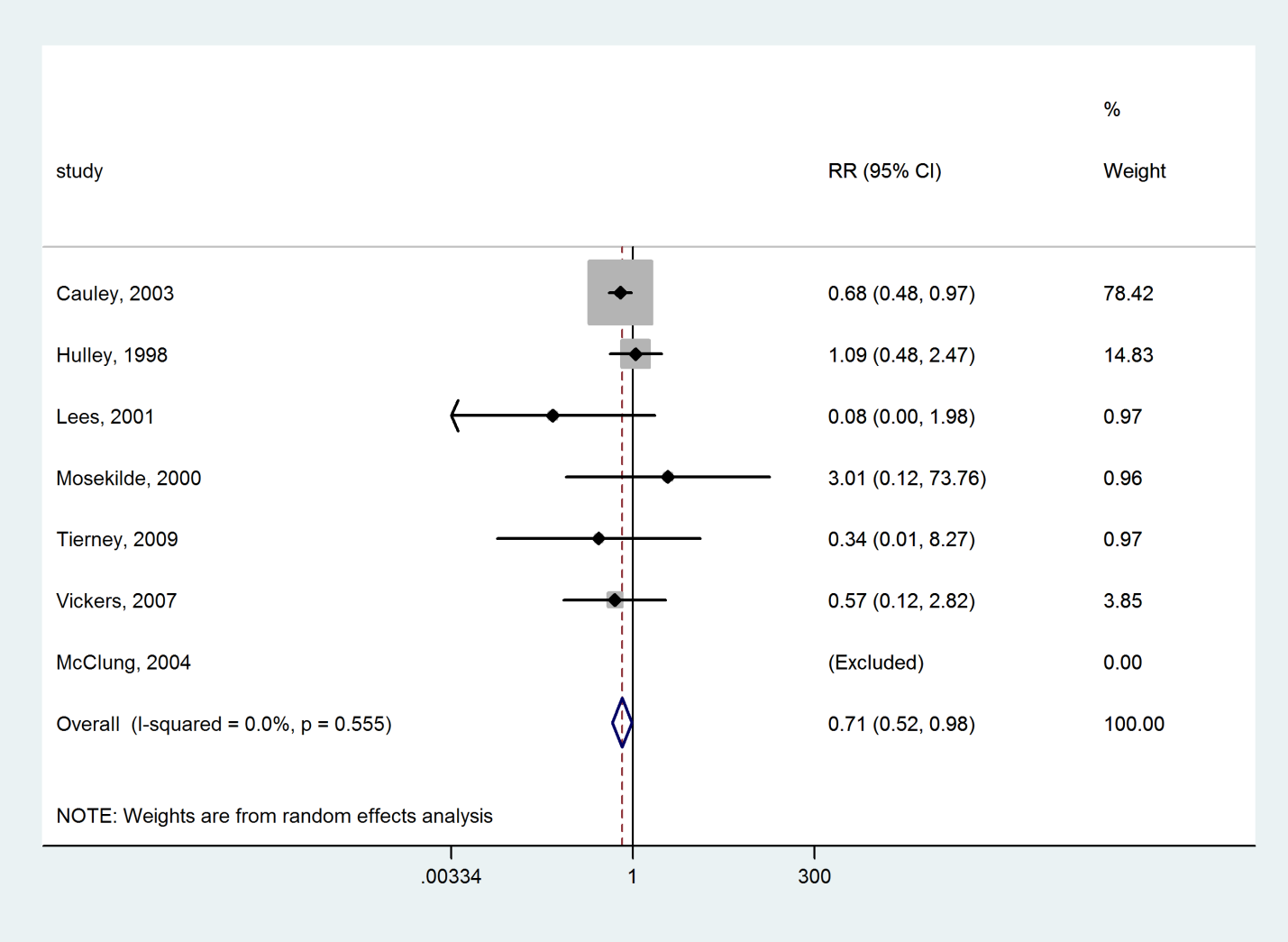
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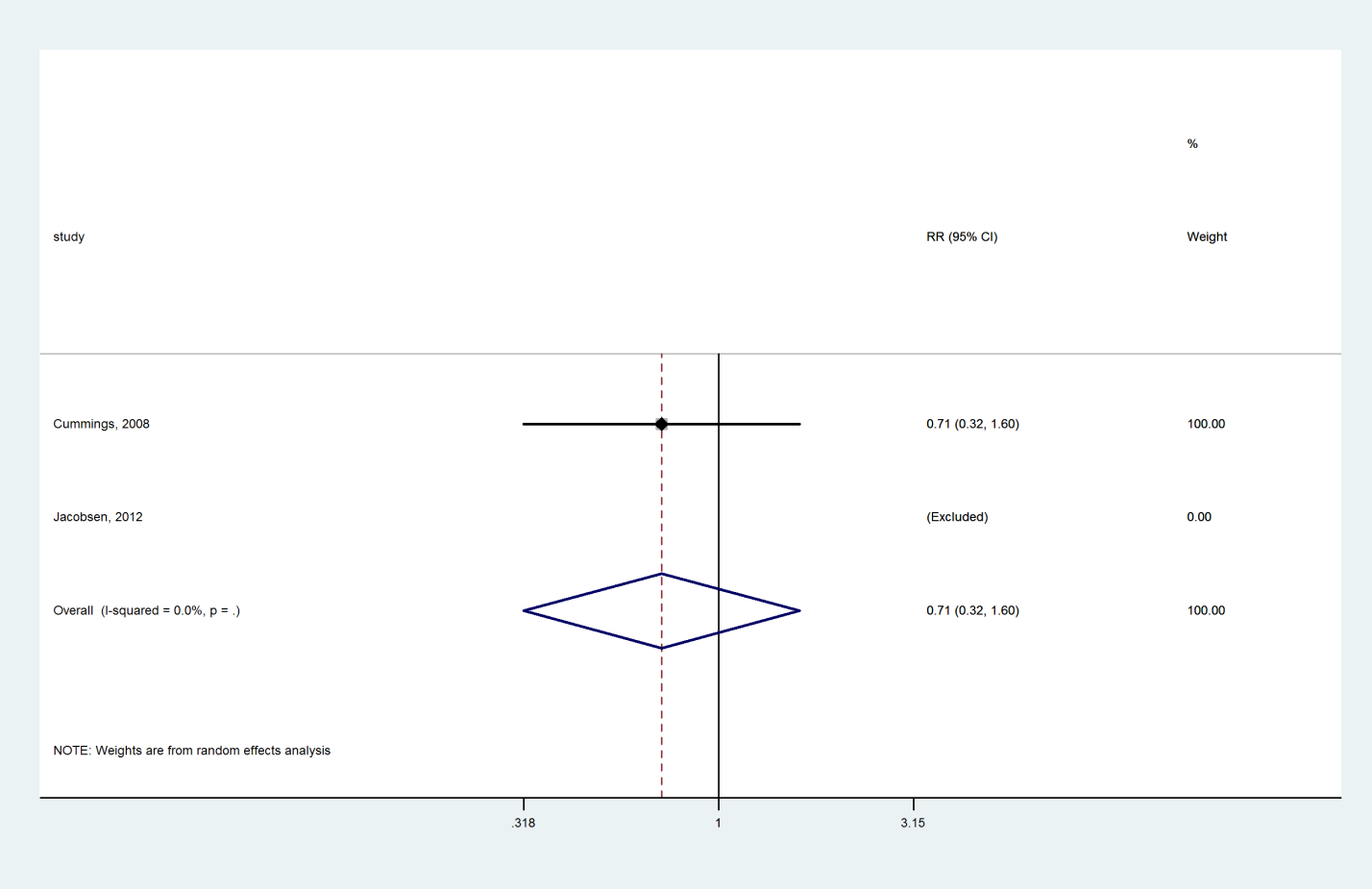
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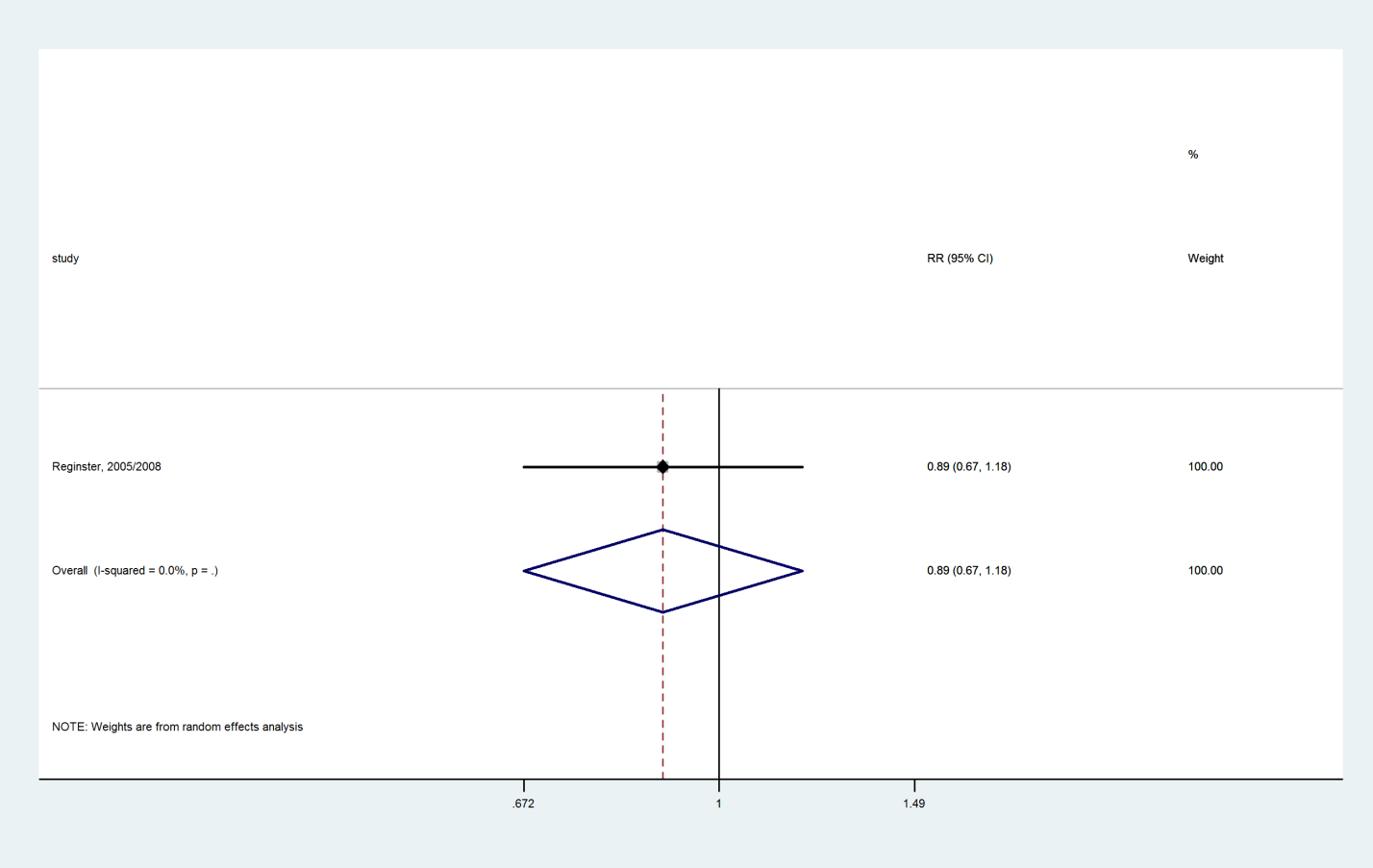
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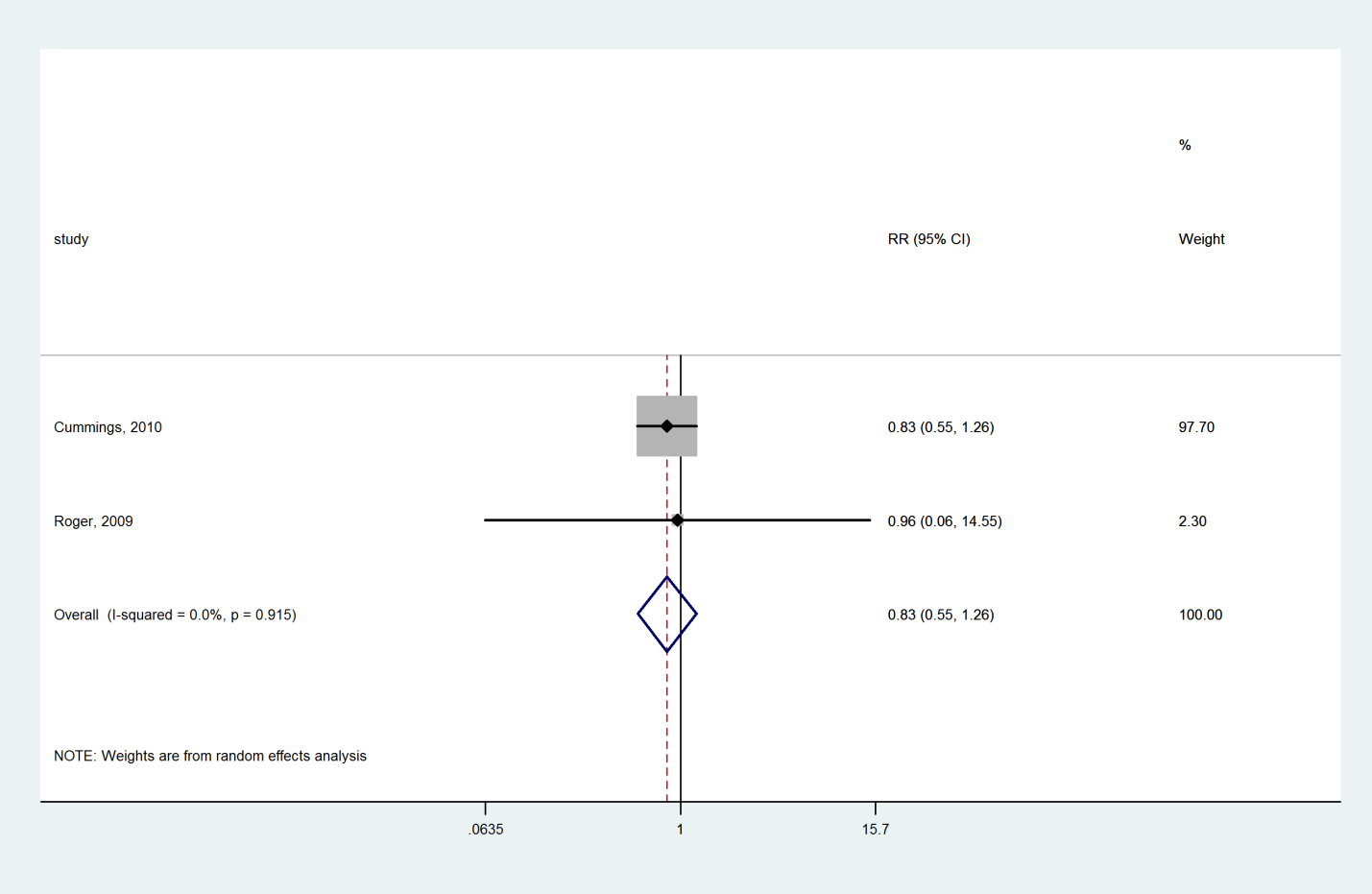
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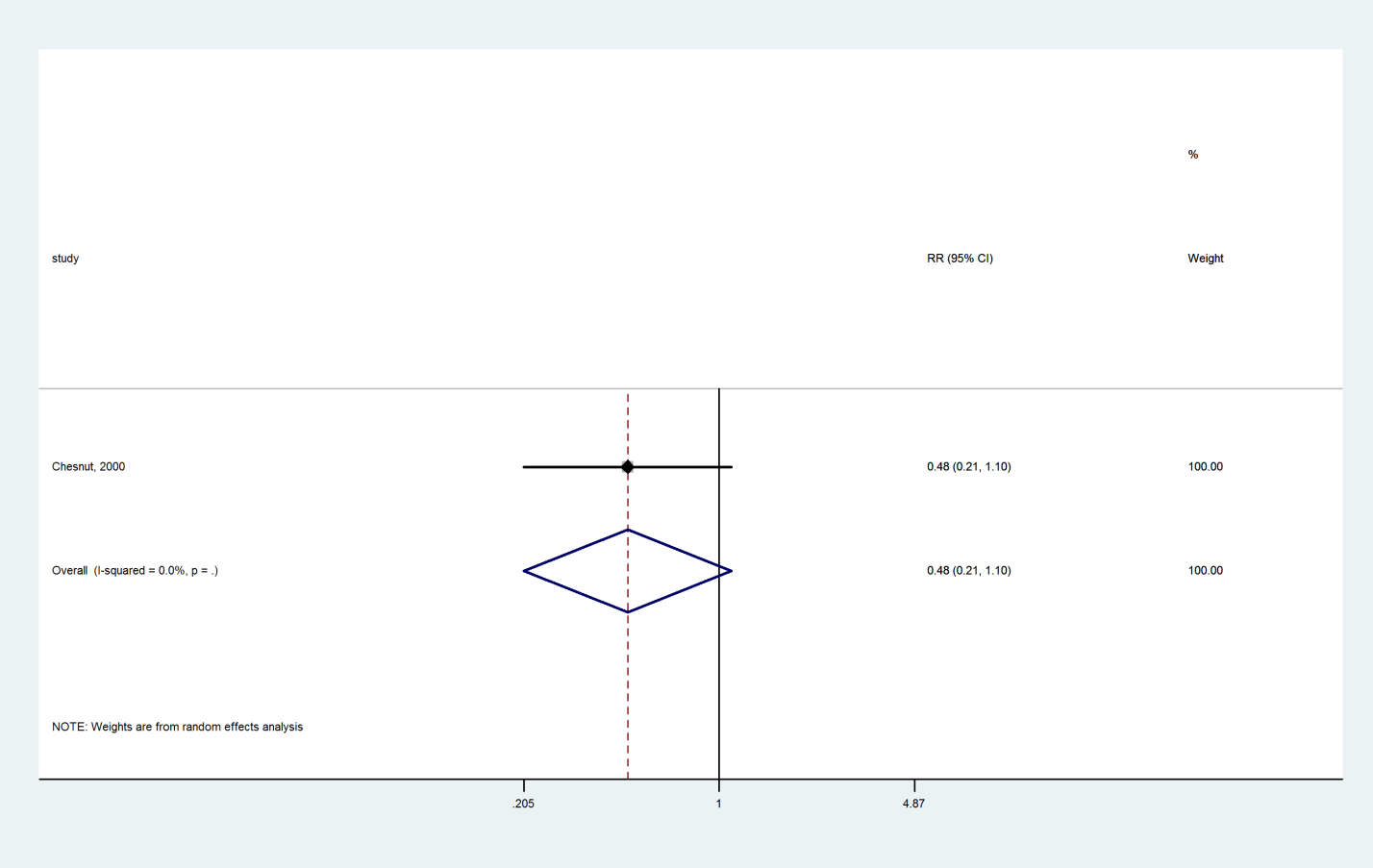
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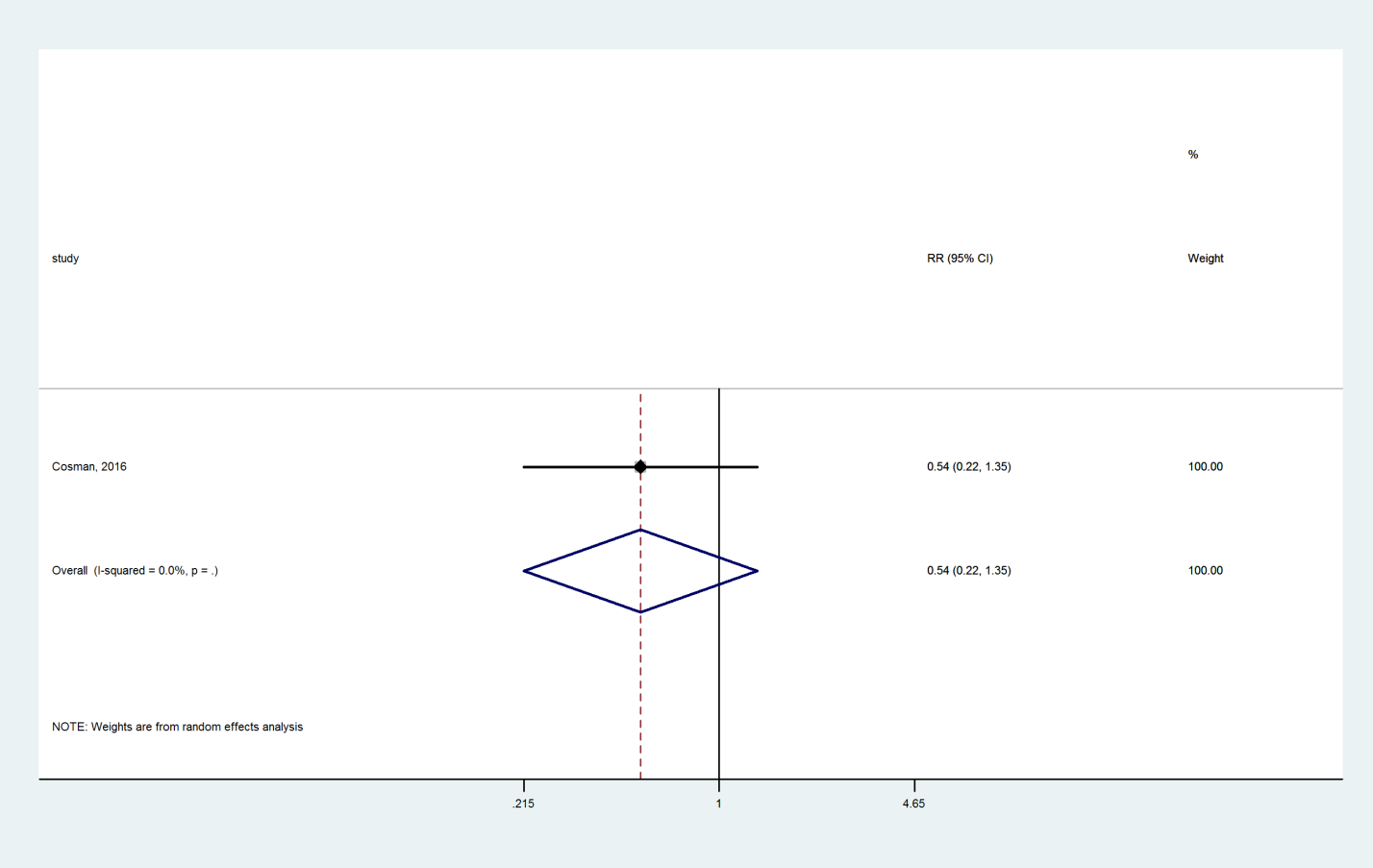
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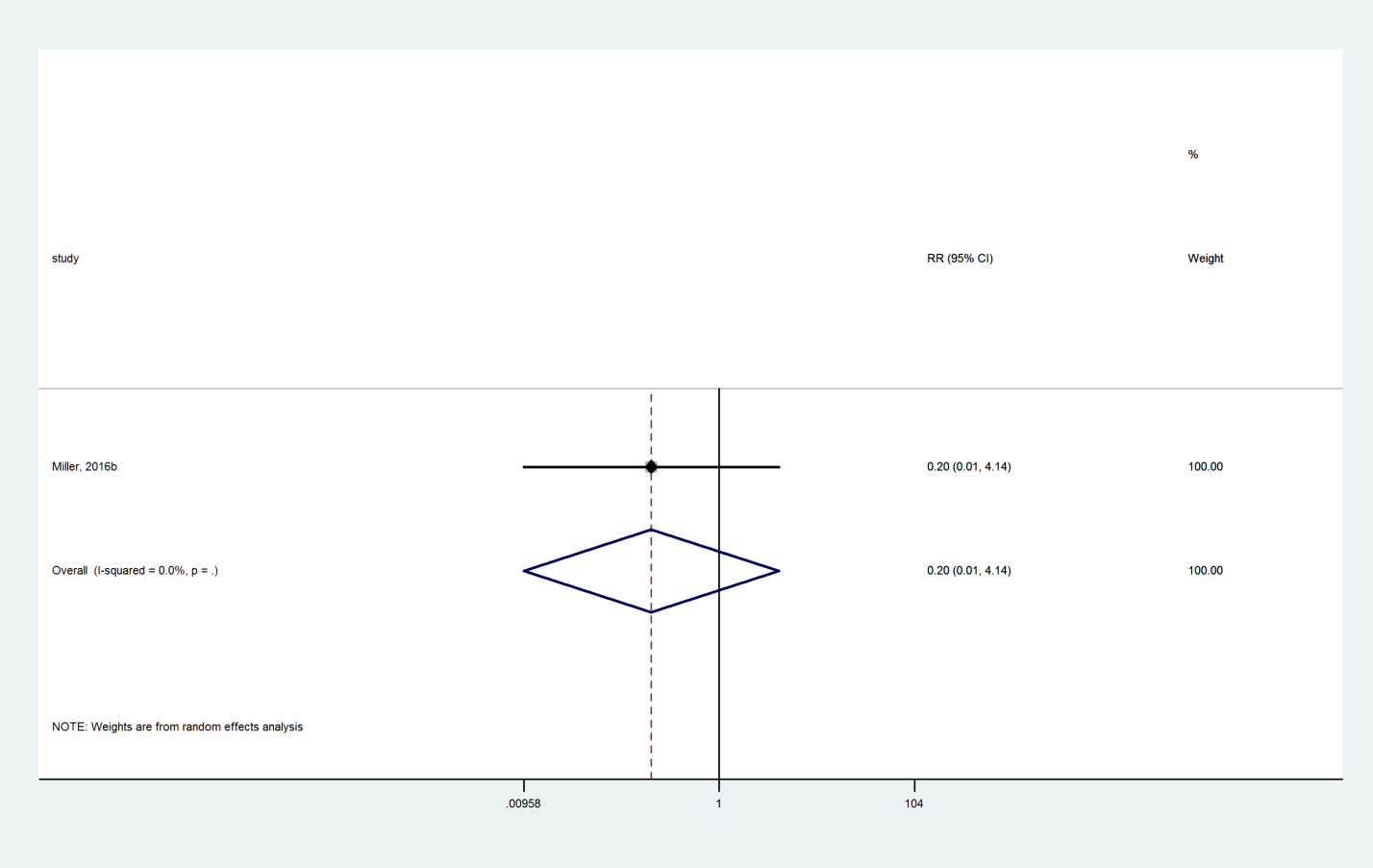
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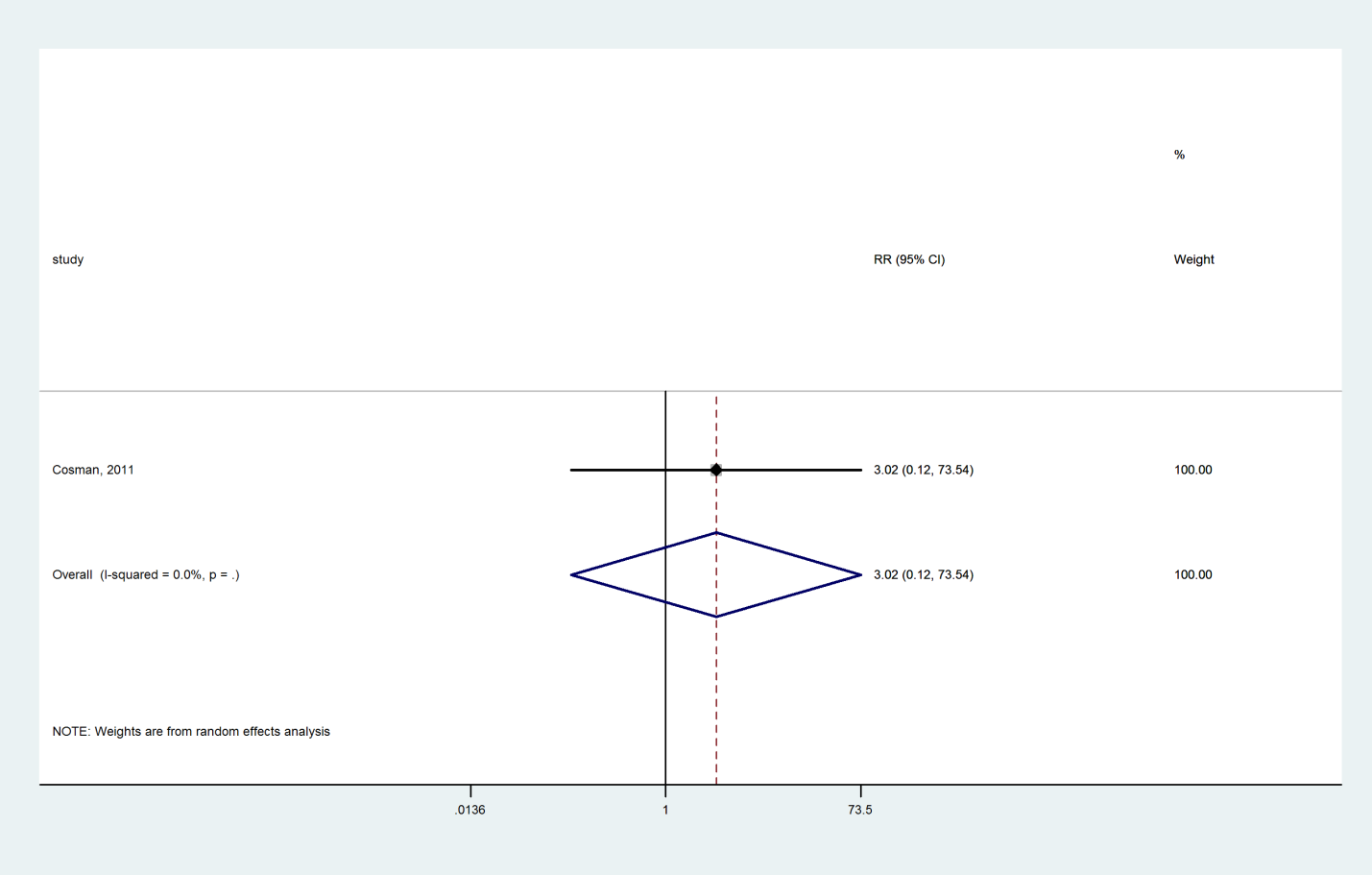
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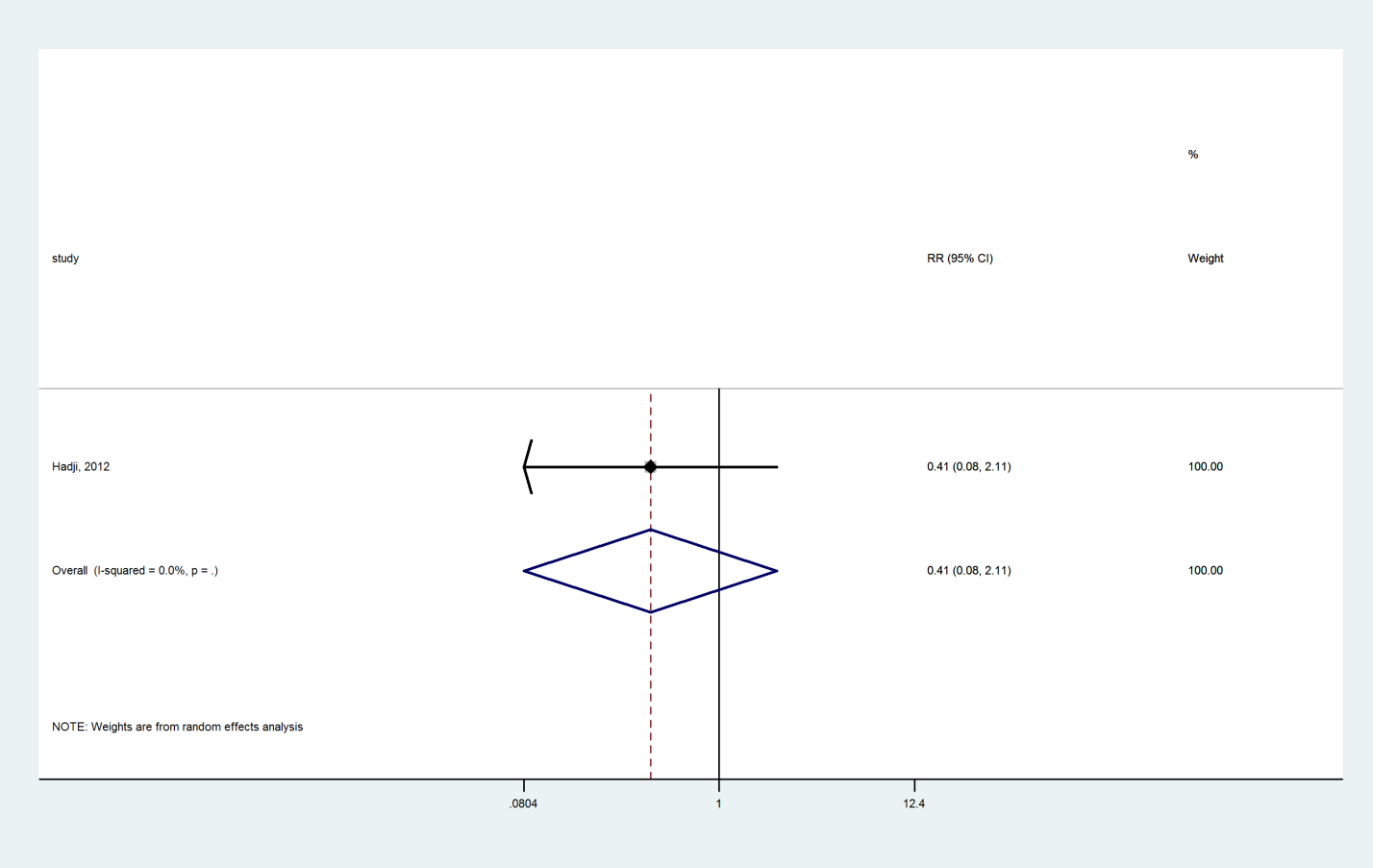
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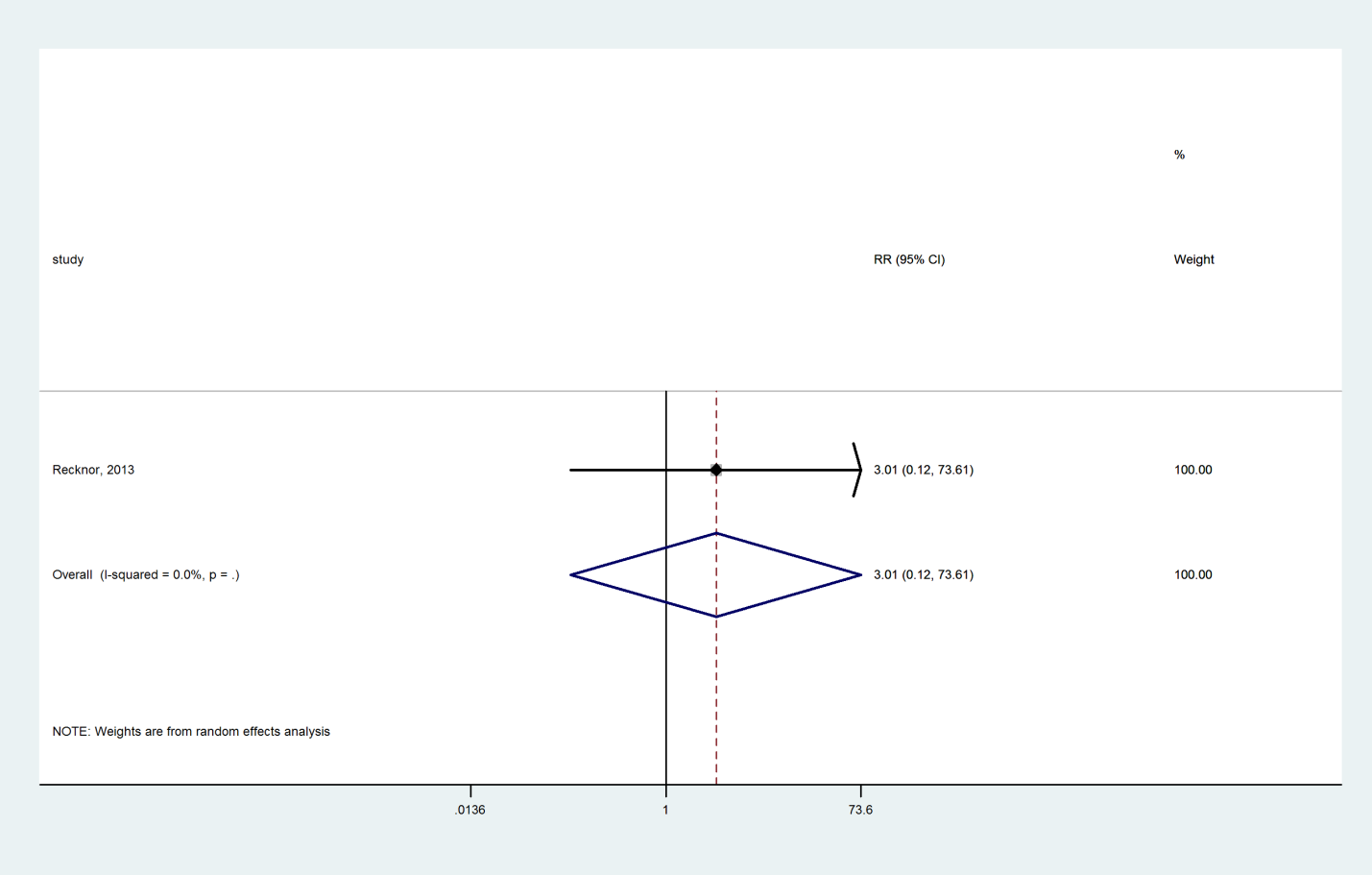
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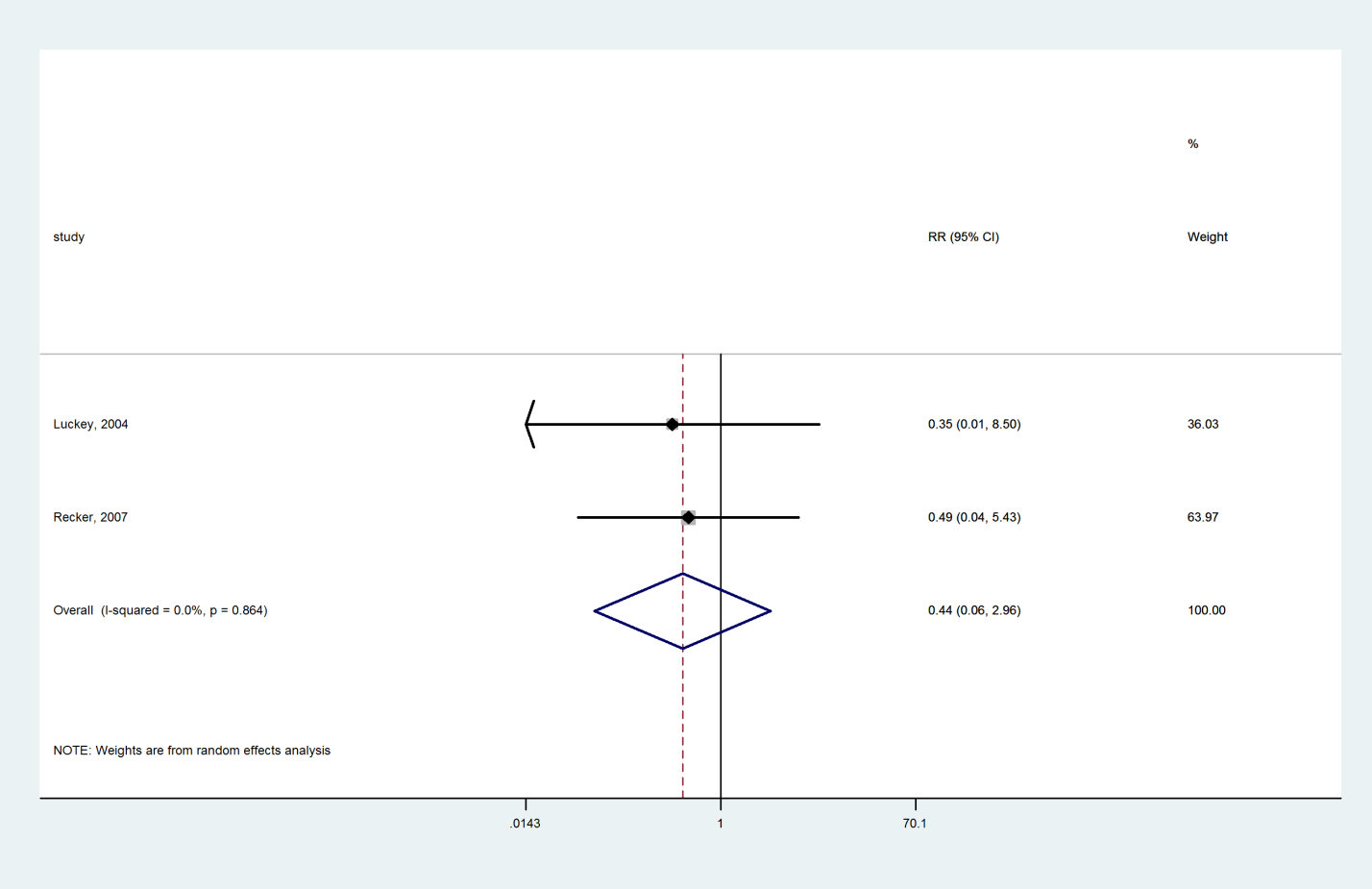
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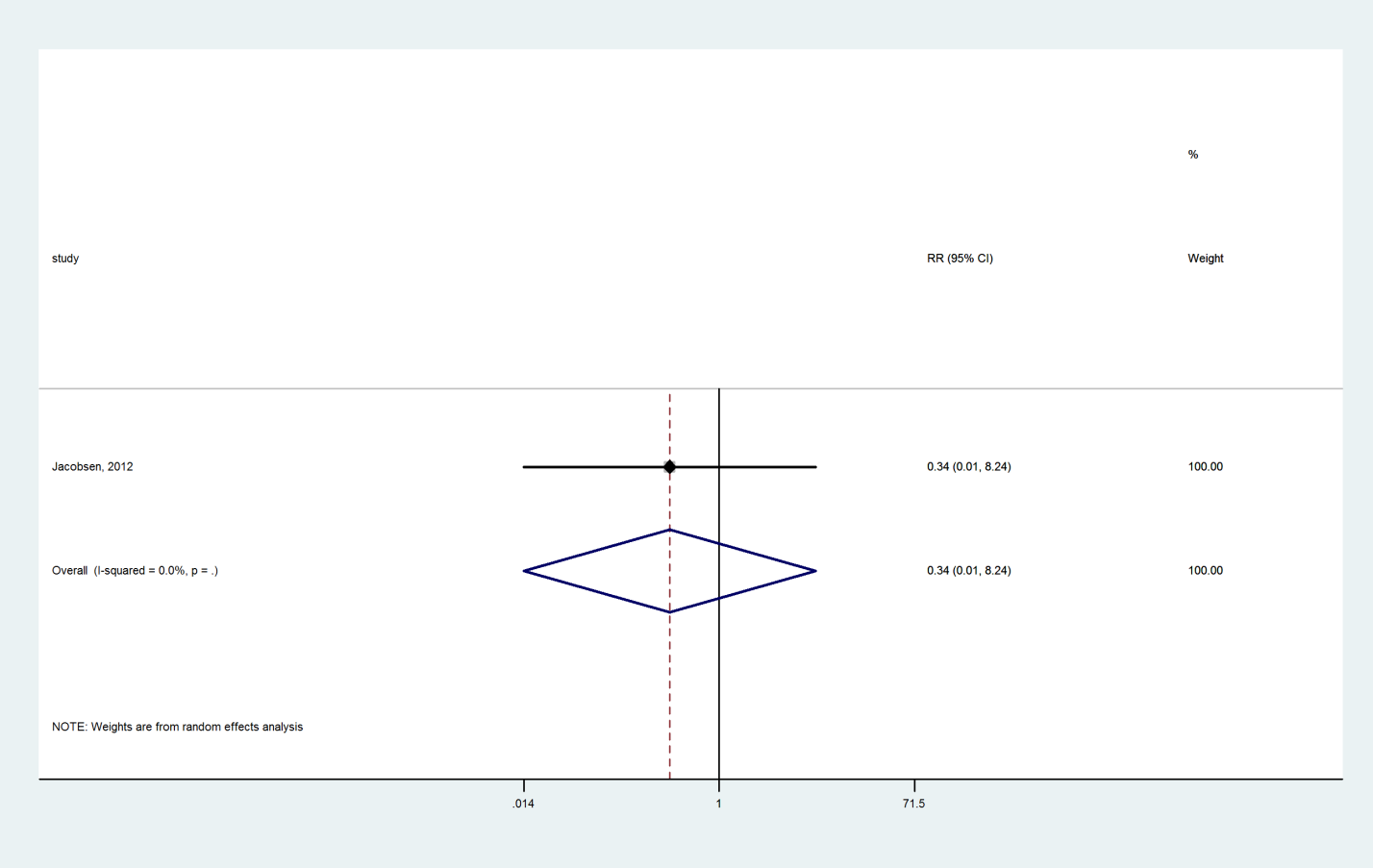
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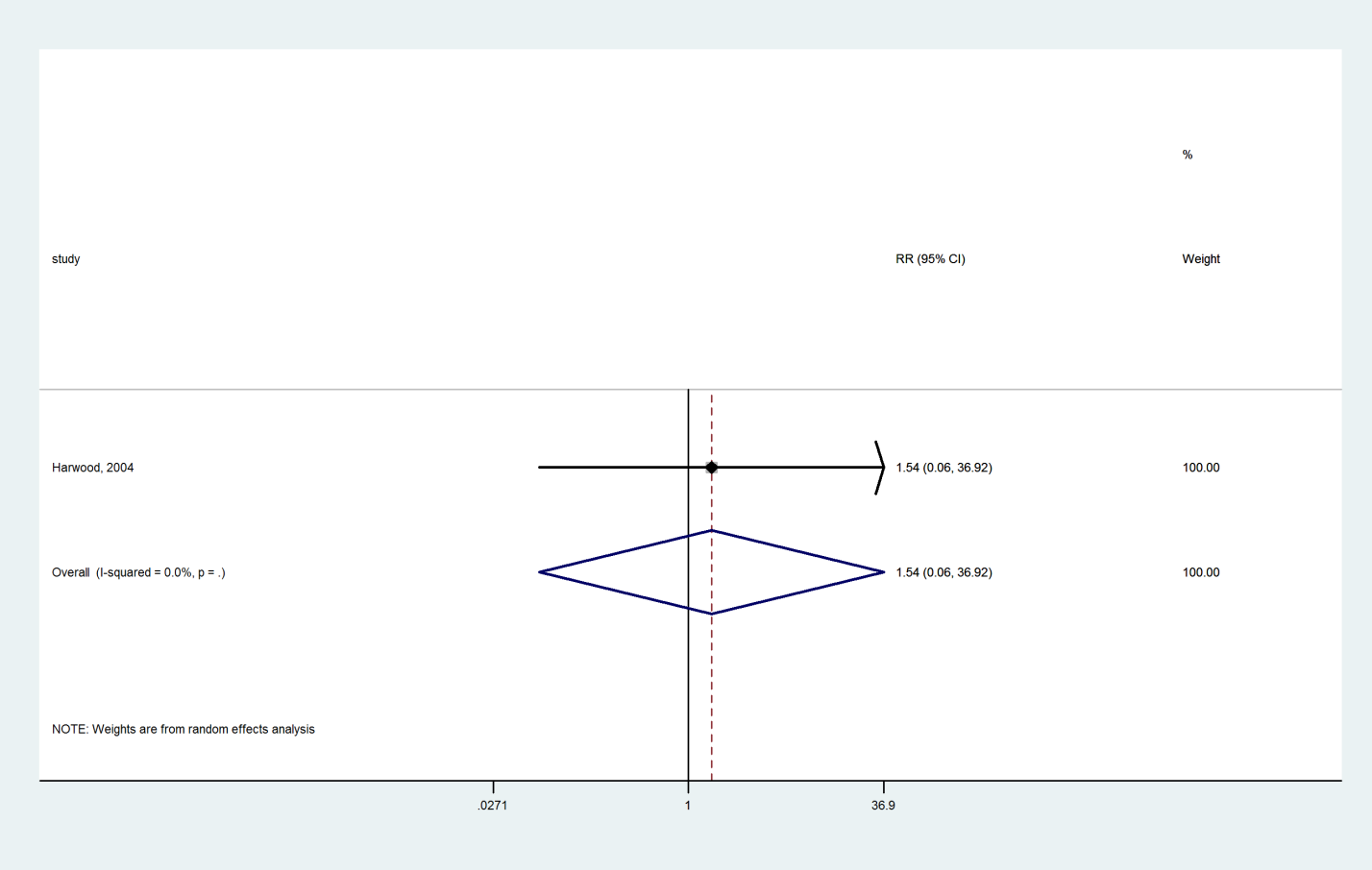
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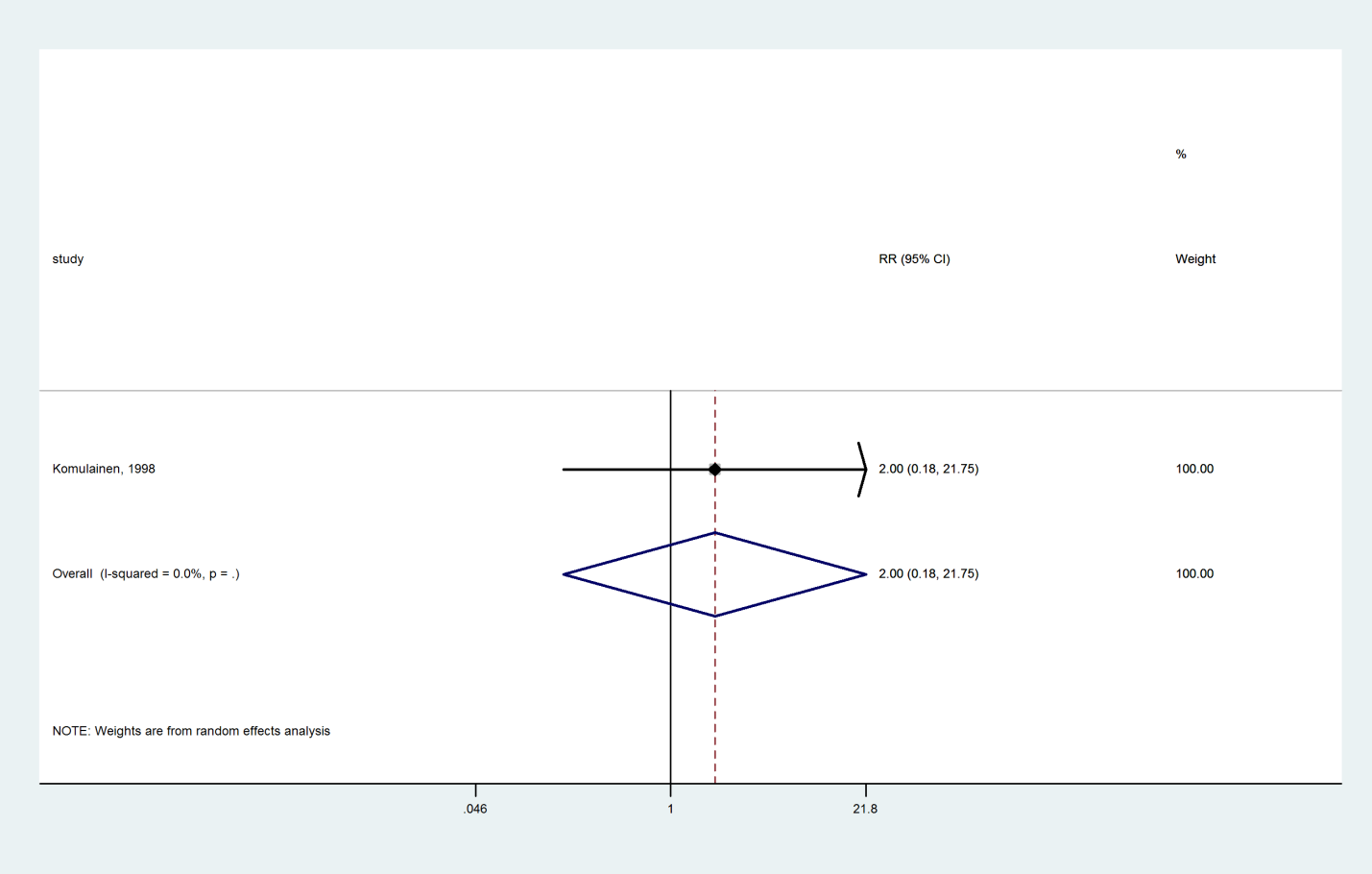
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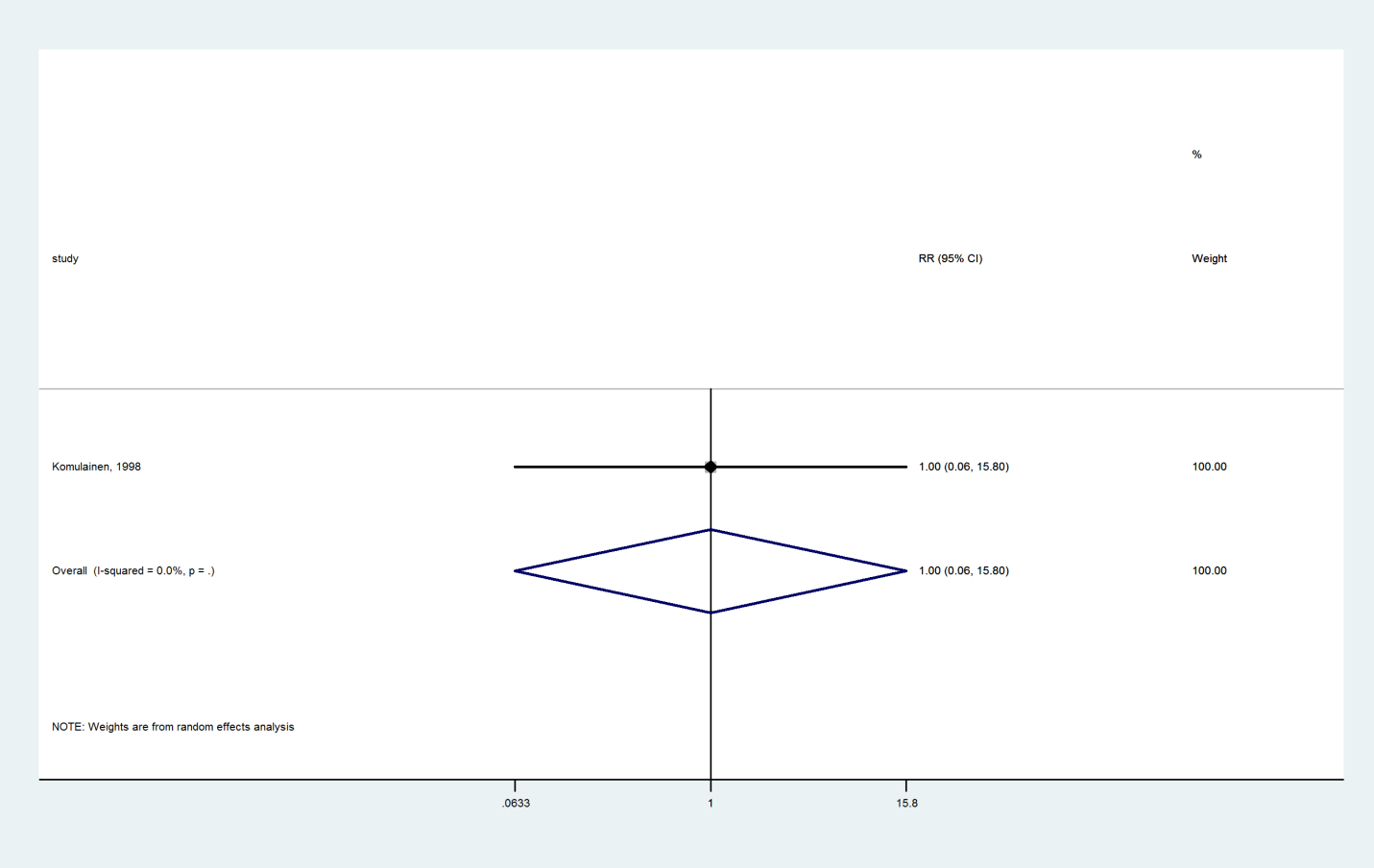
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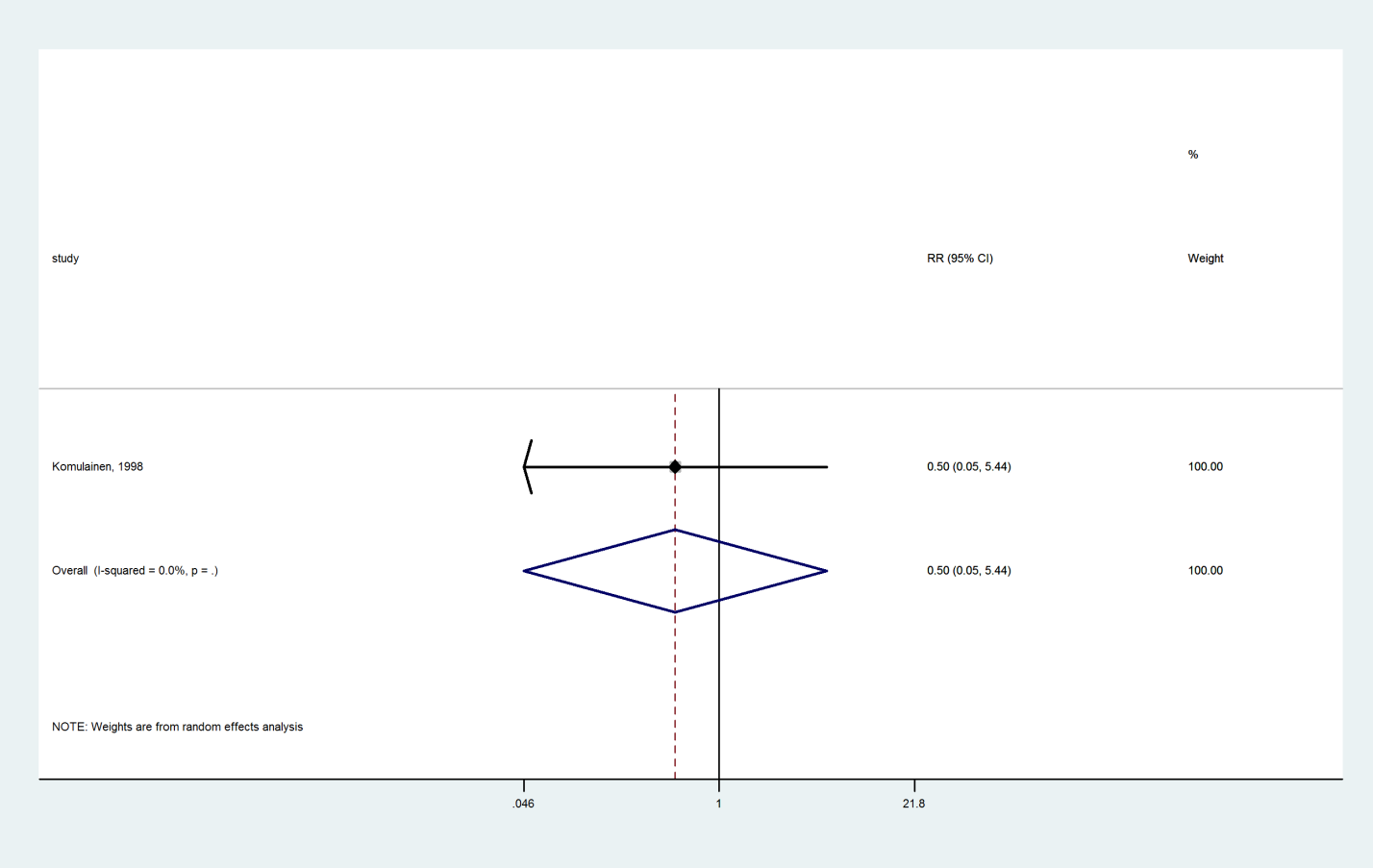
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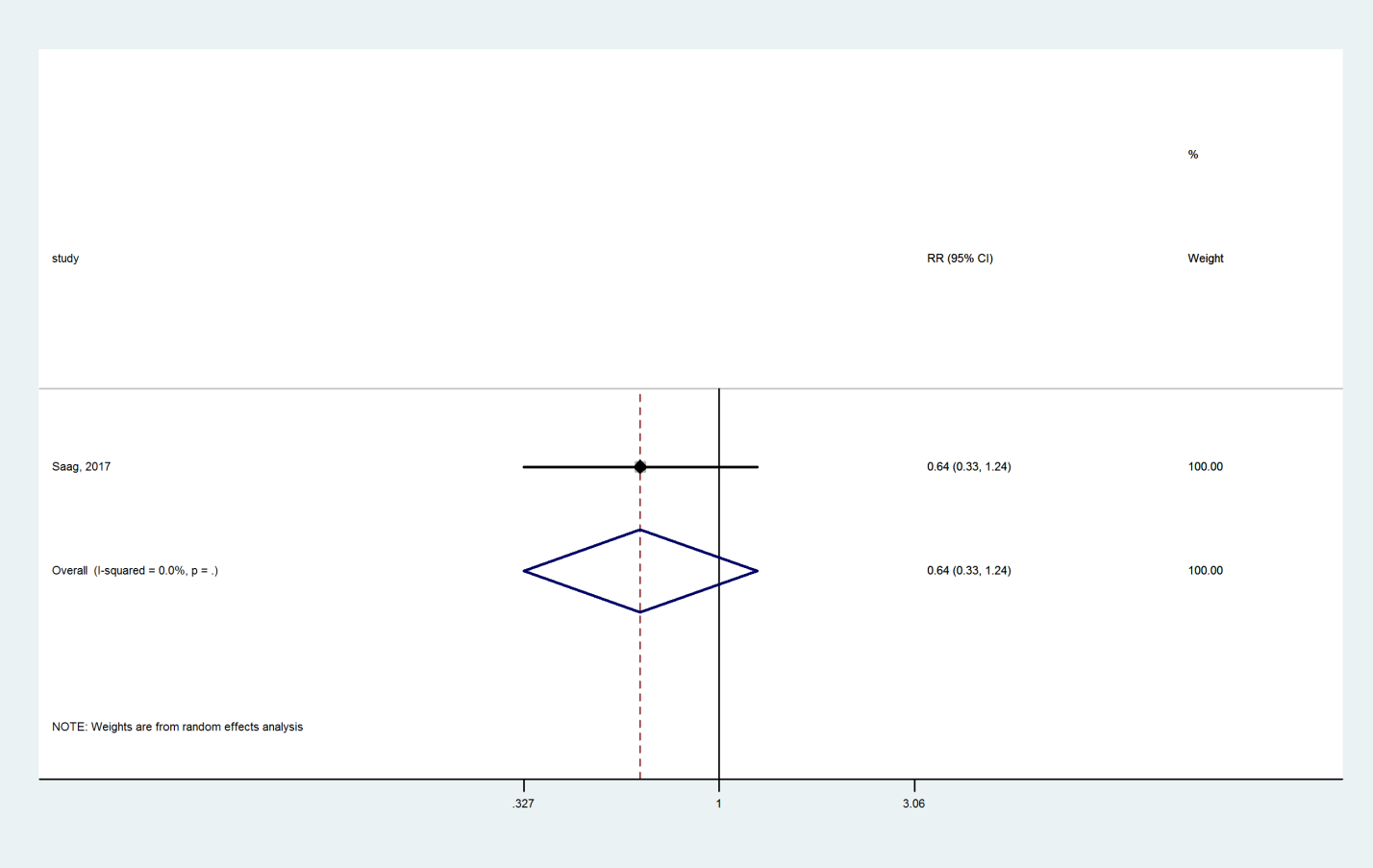
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### Hormone therapy compared with Calcium

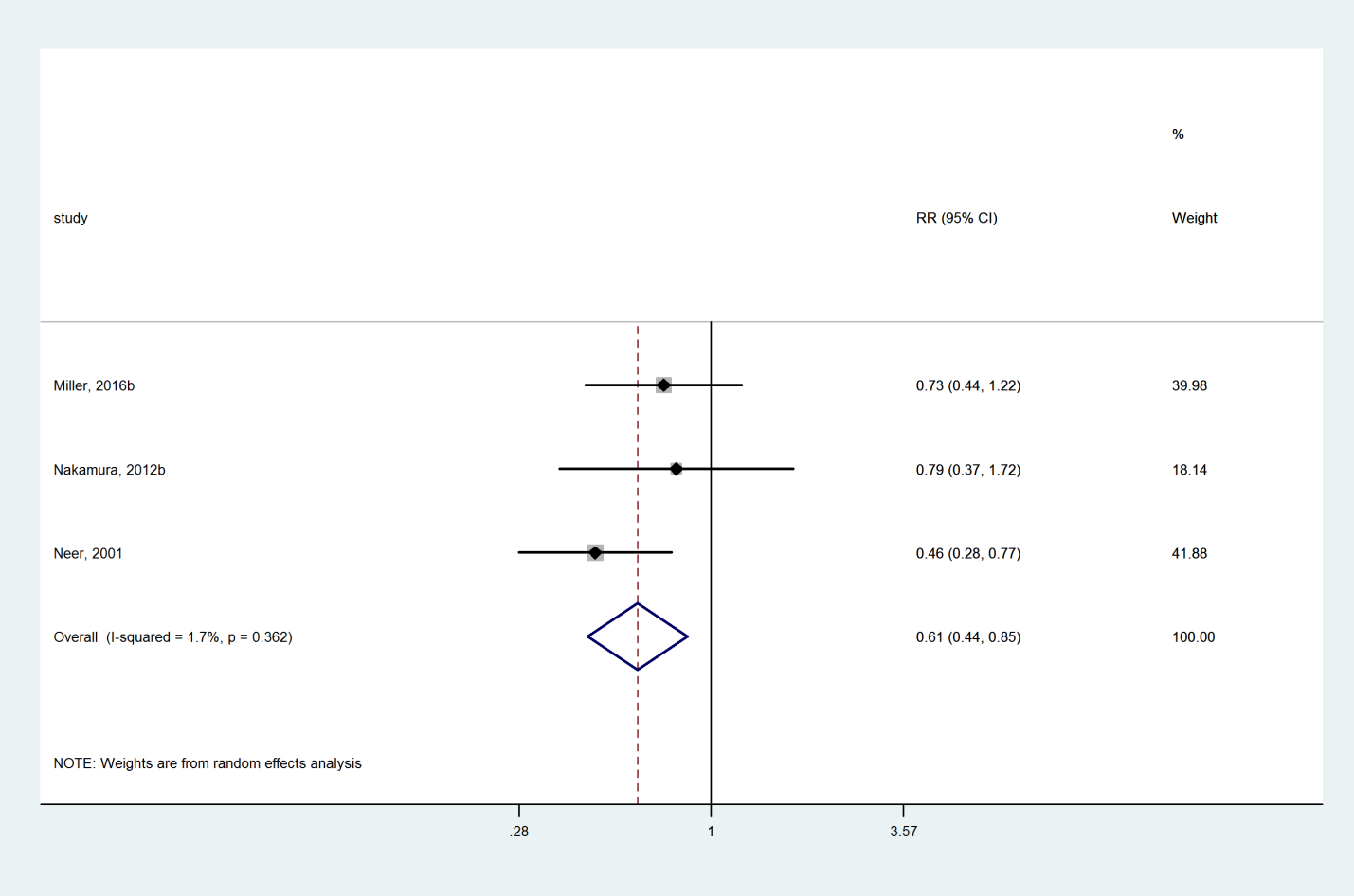


### Romosozumab compared with Alendronate

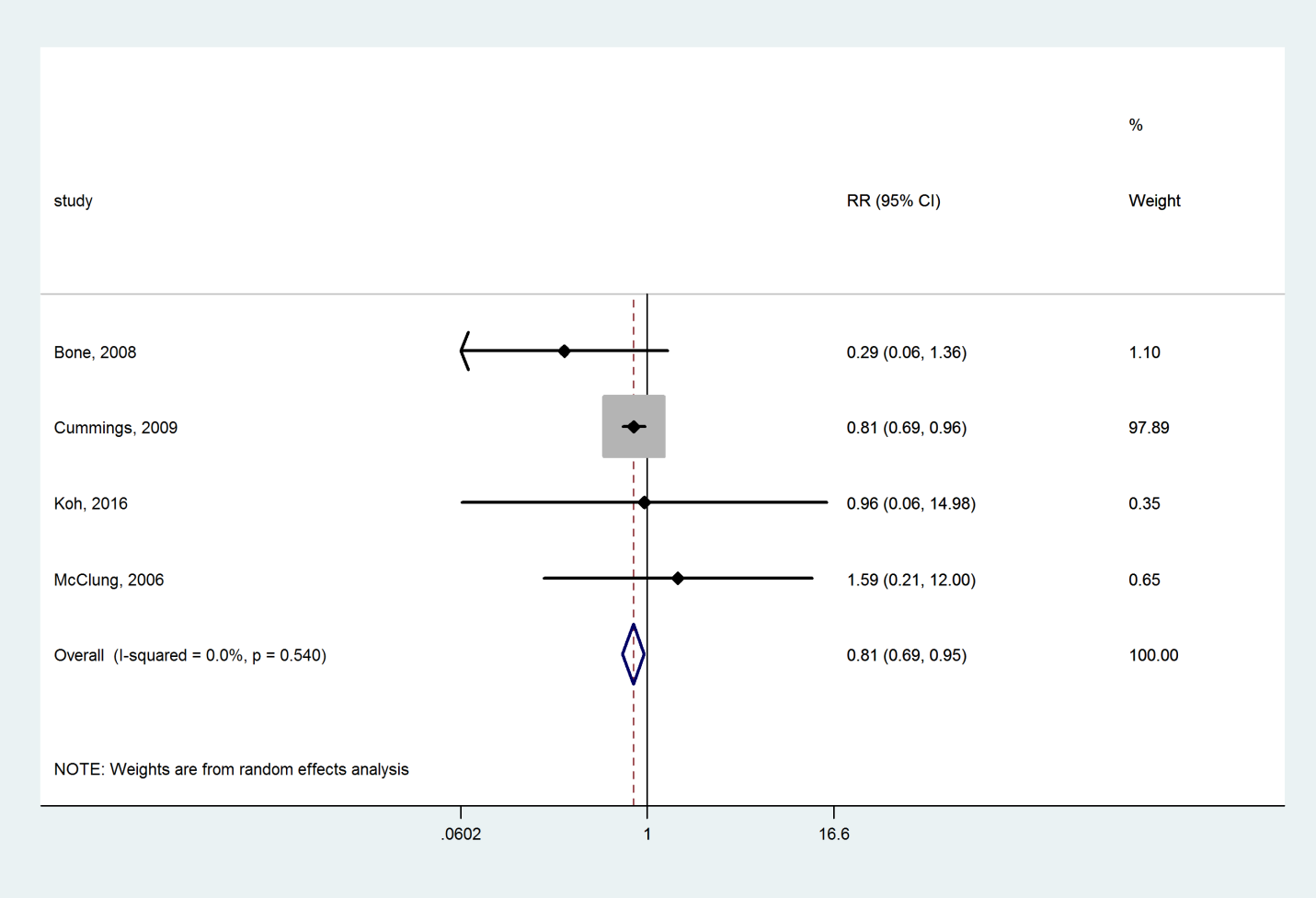


## Nonvertebral Fracture

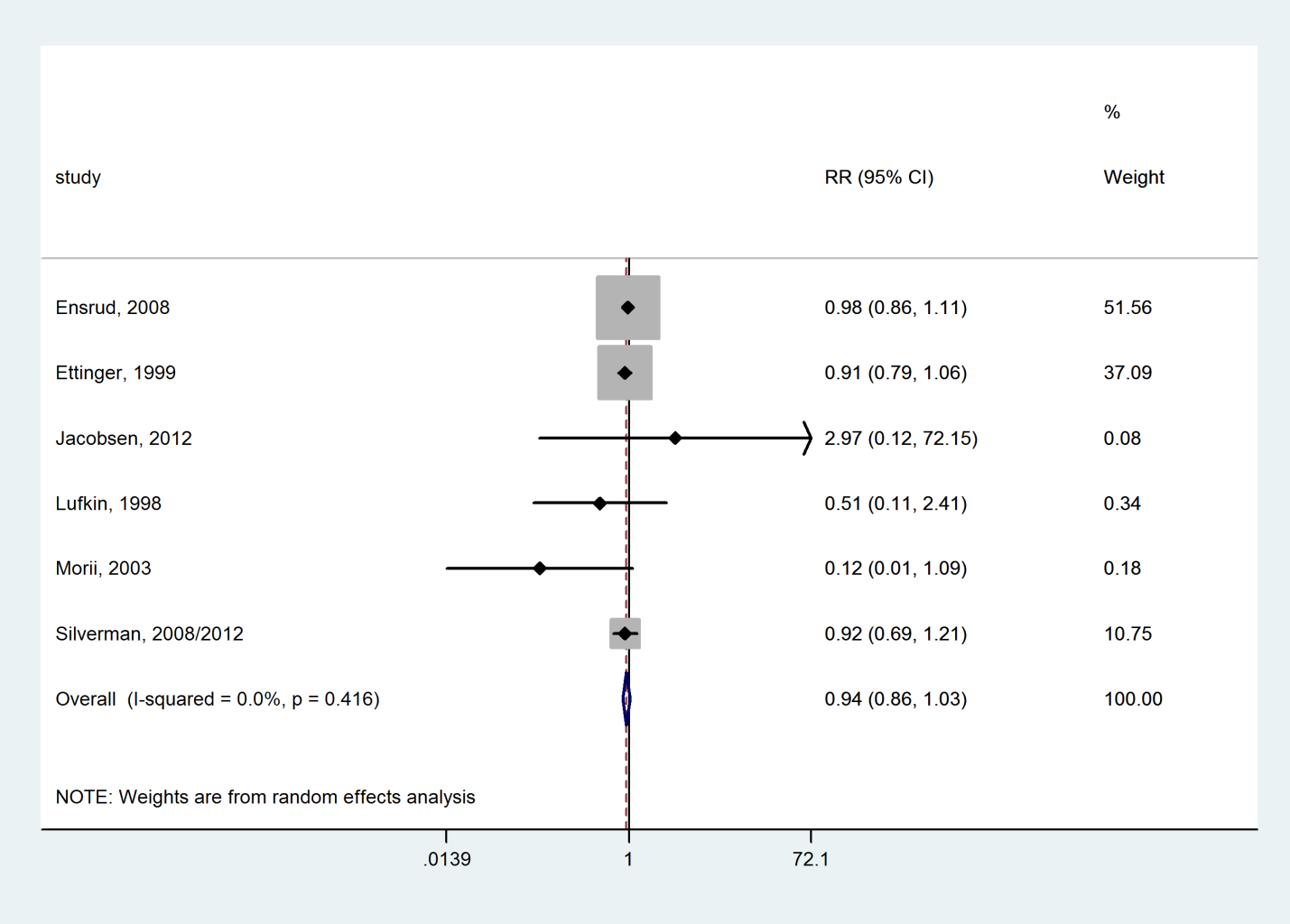
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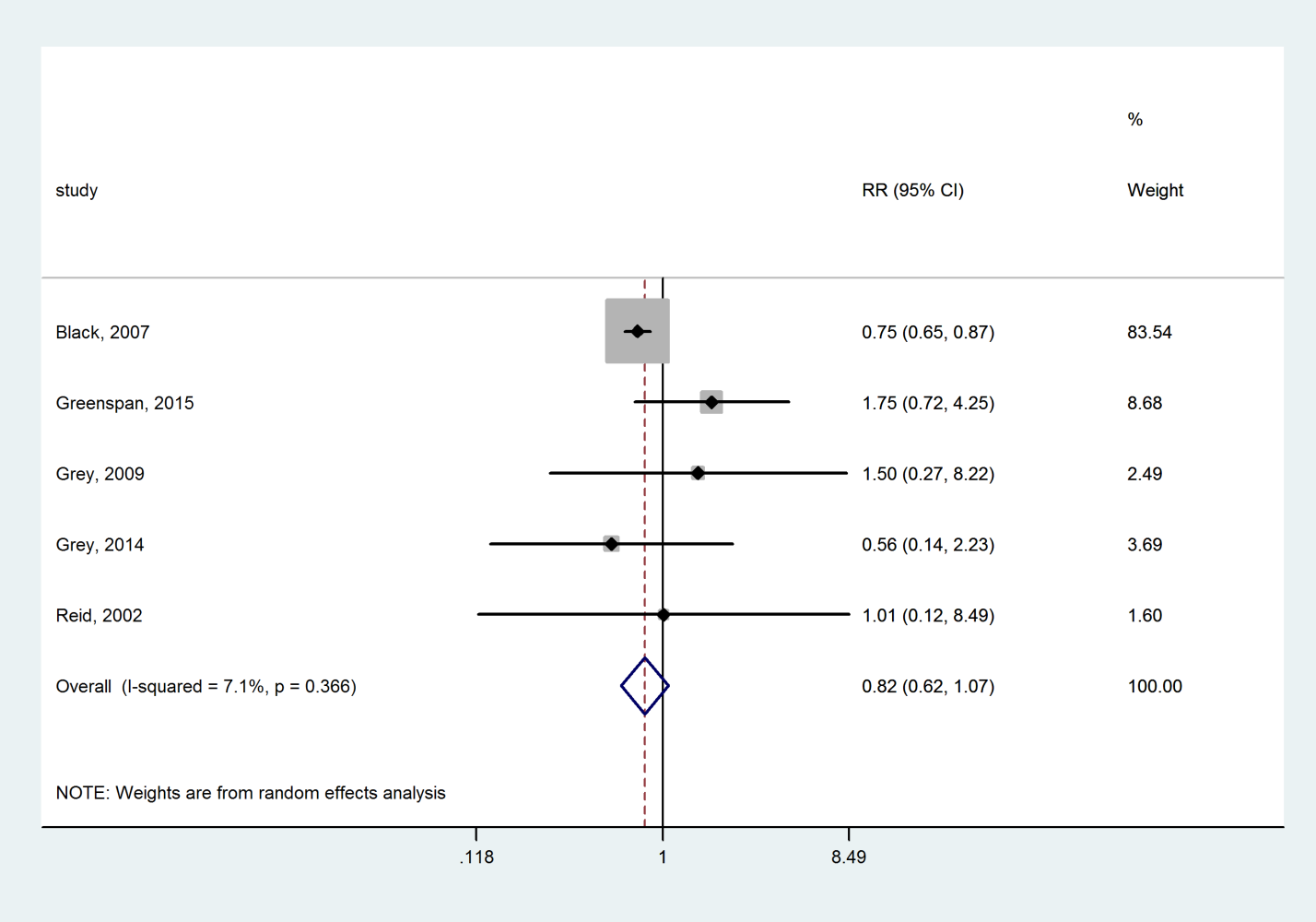
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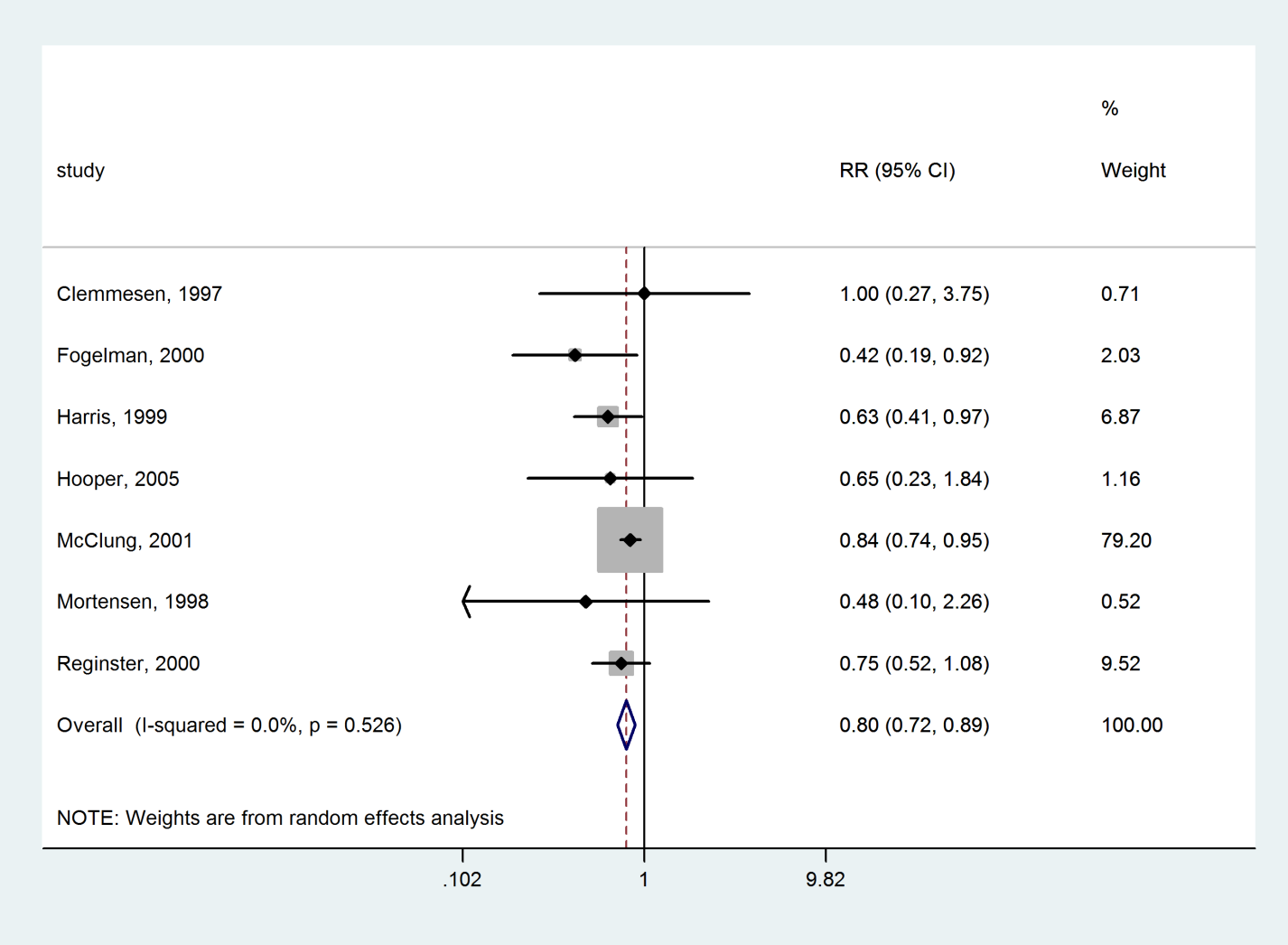
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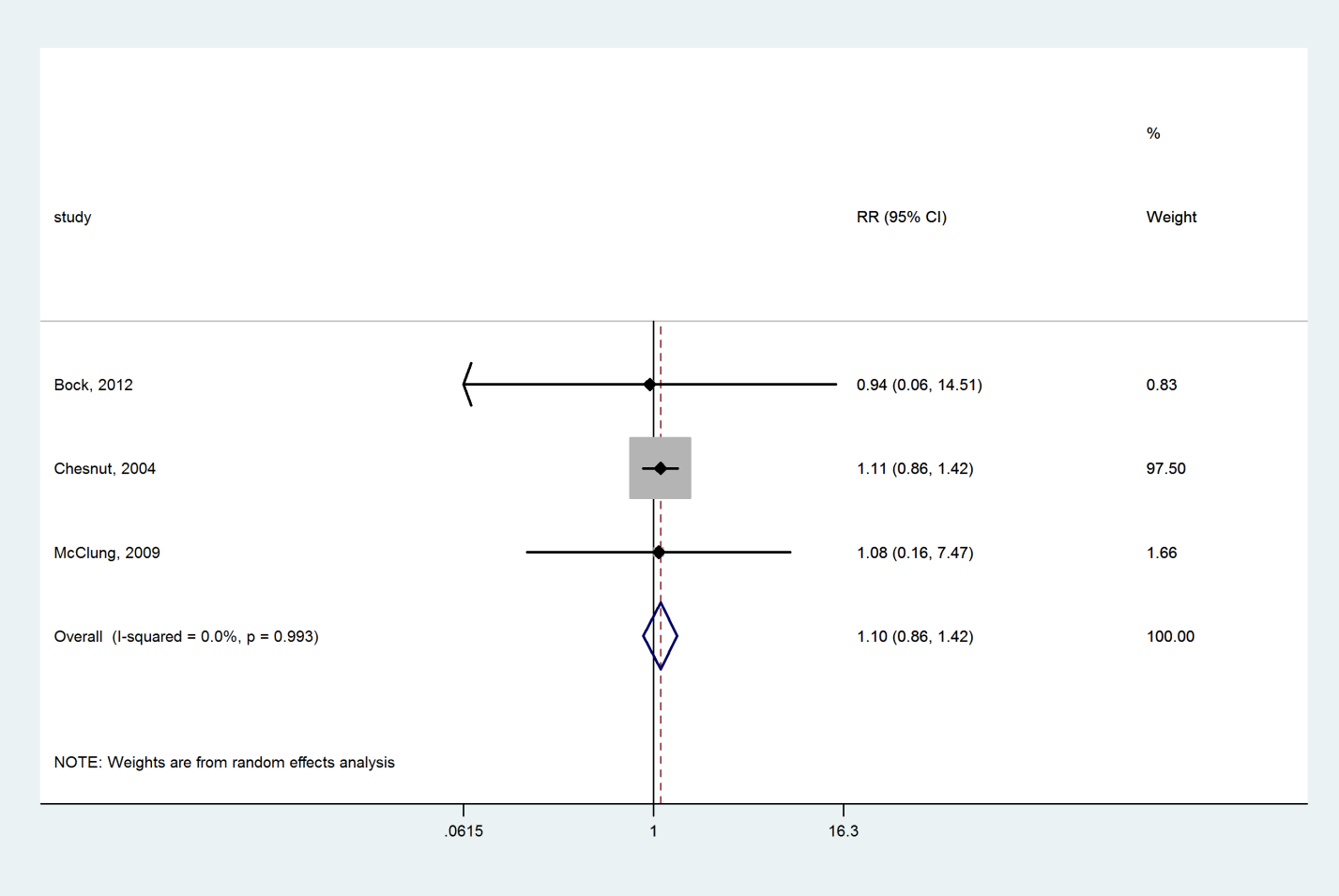
### Zoledronate compared with Placebo



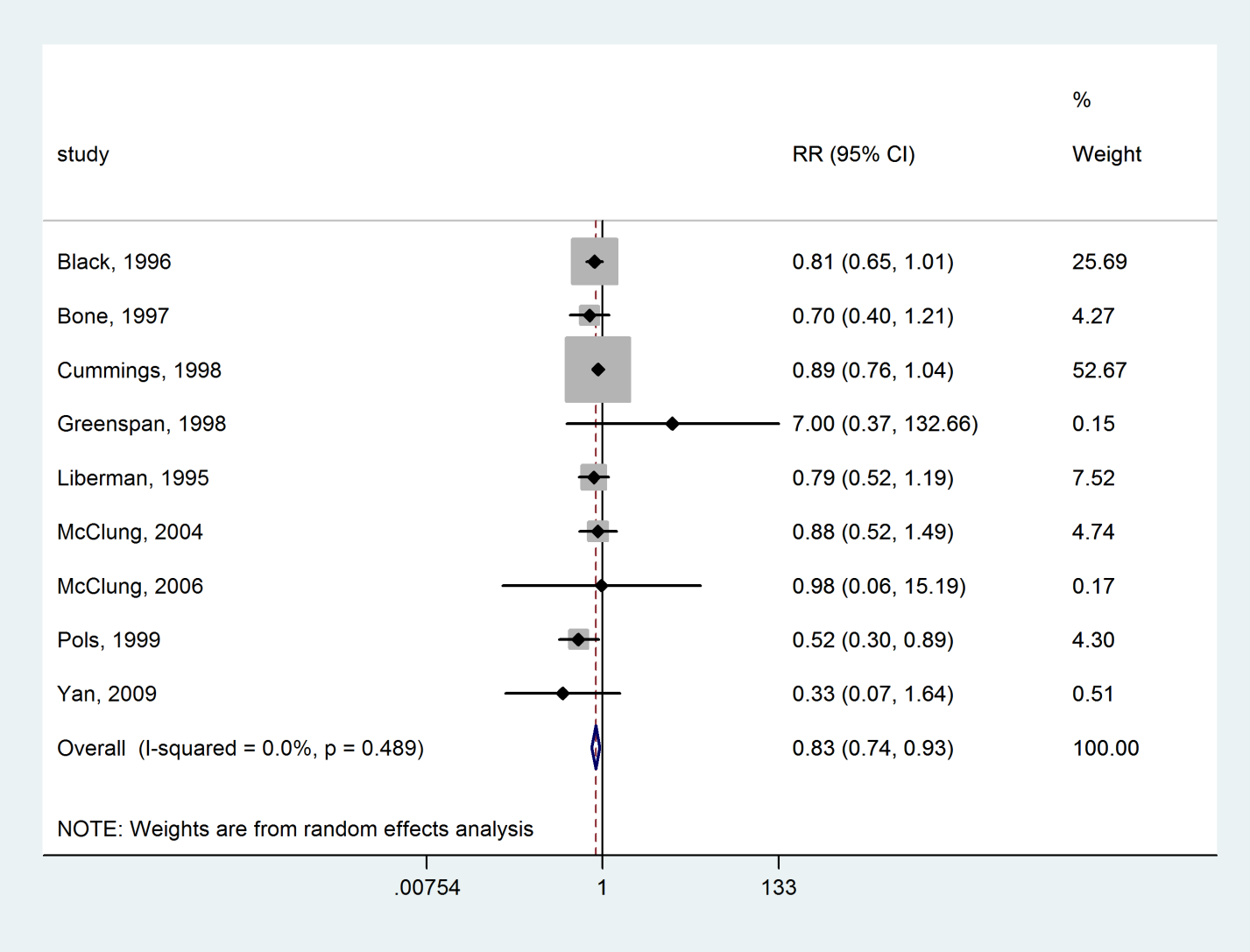
### Risedronate compared with Placebo



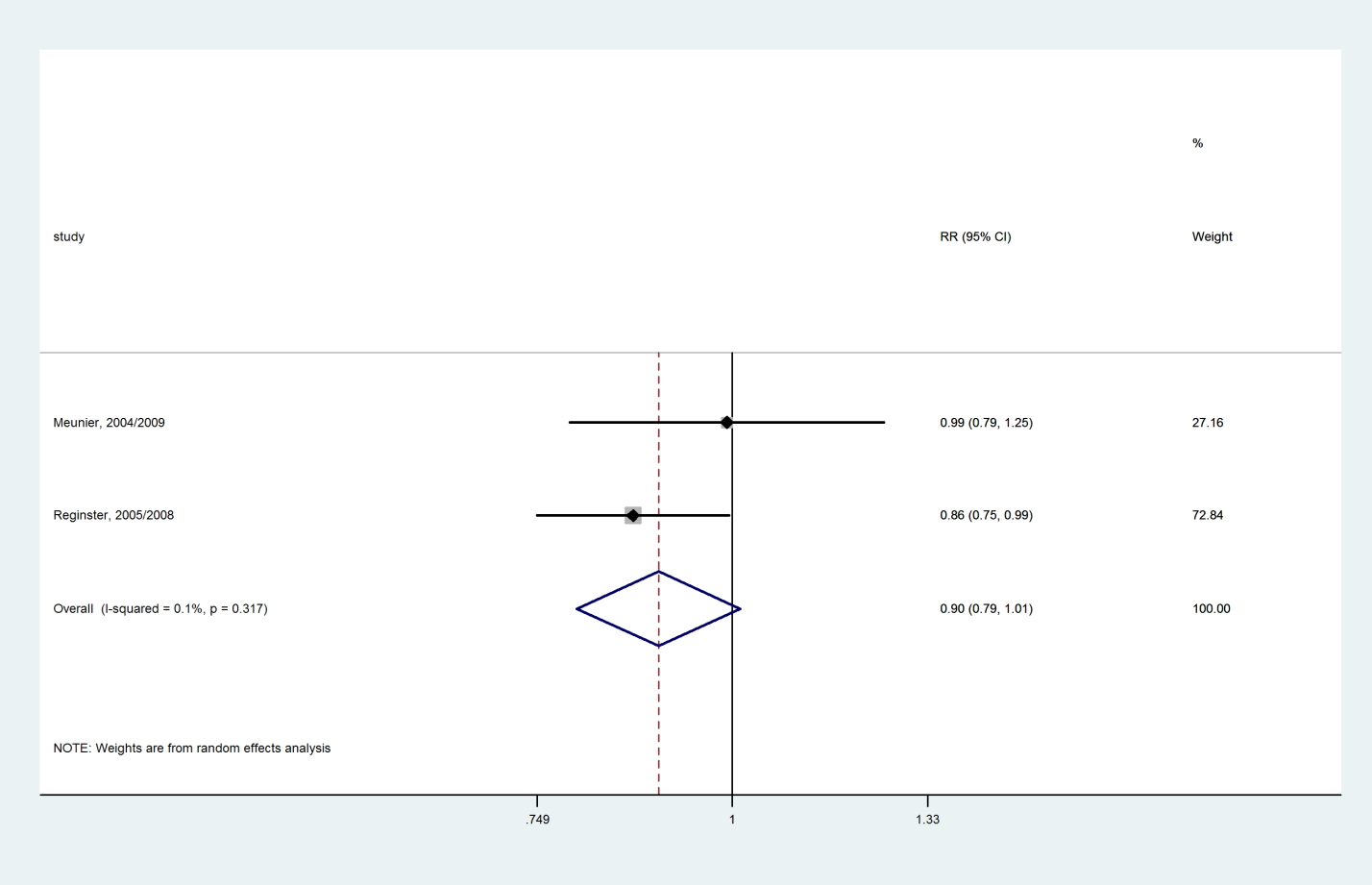
### Ibandronate compared with Placebo



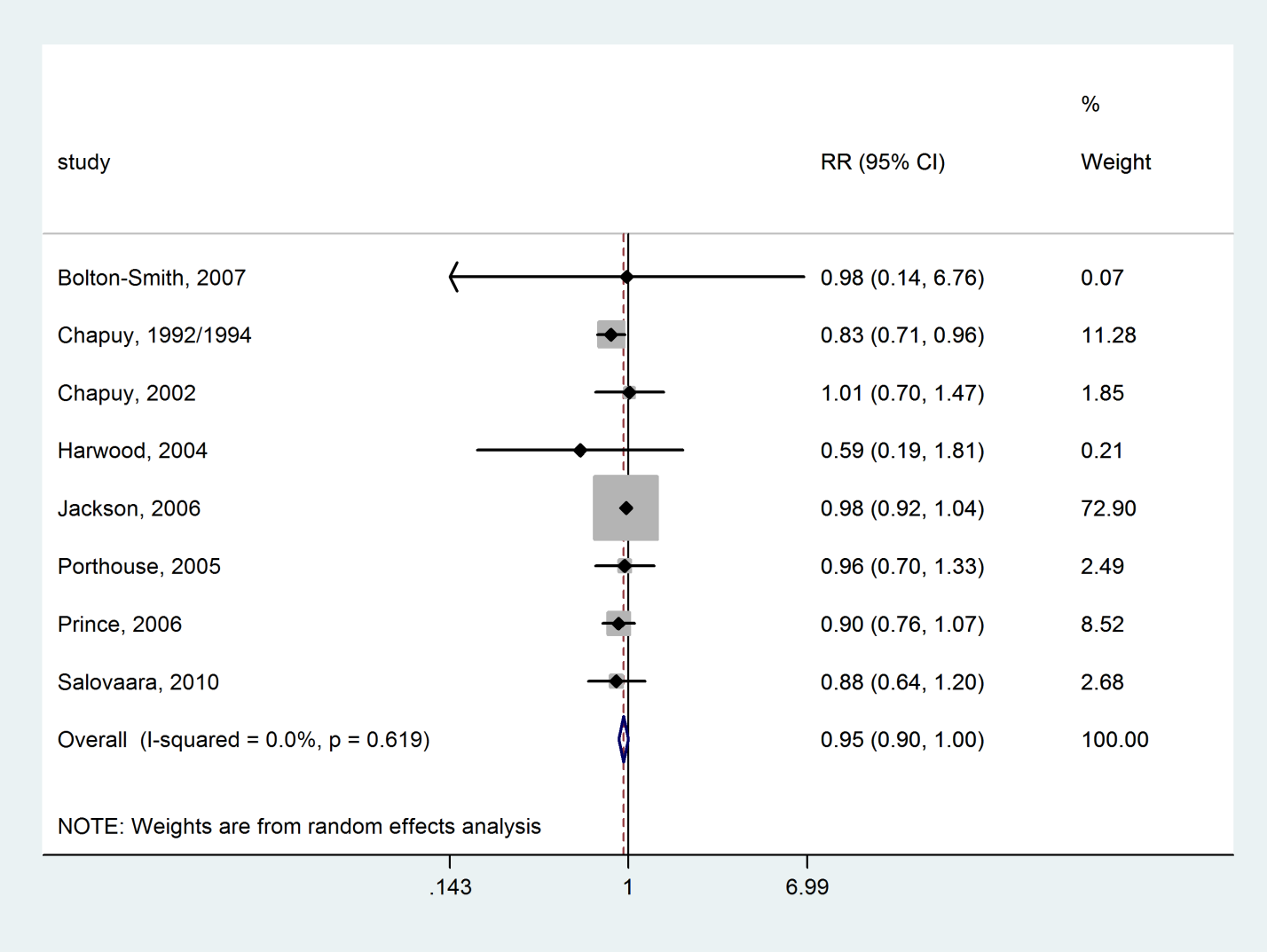
### Alendronate compared with Placebo



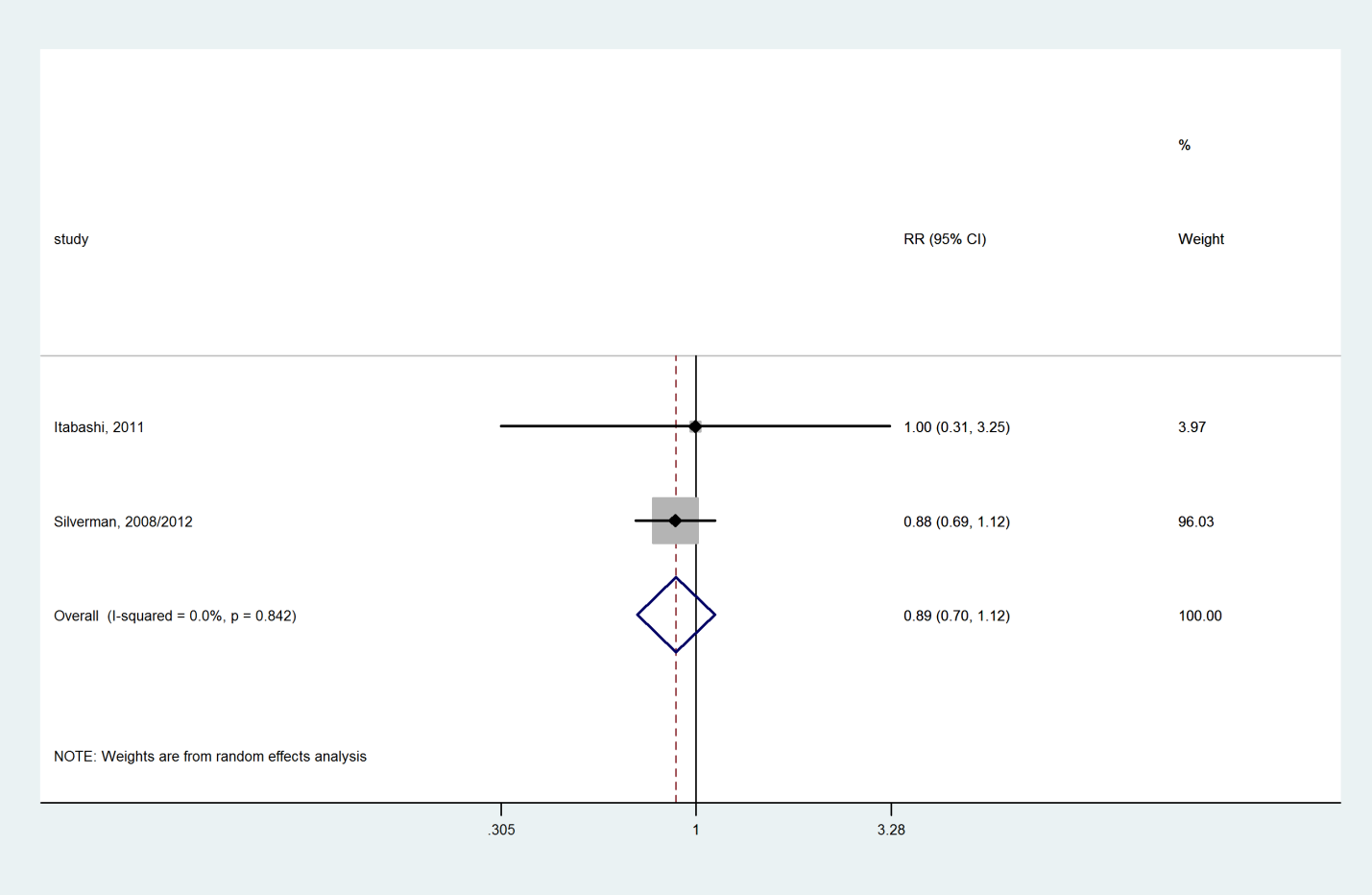
### Strontium ranelate compared with Placebo



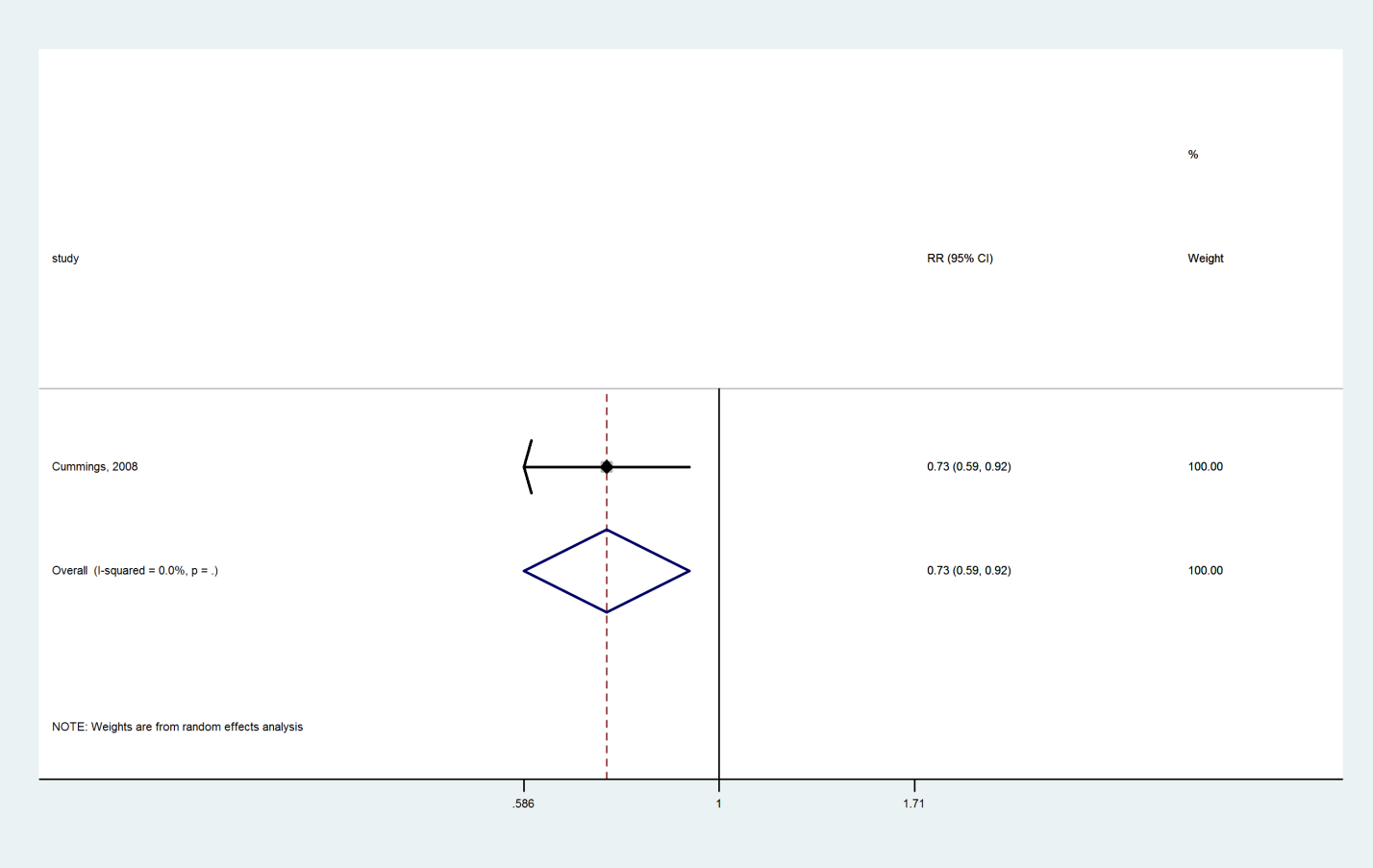
### Vitamin D+Calcium compared with Placebo



### Bazedoxifene compared with Placebo



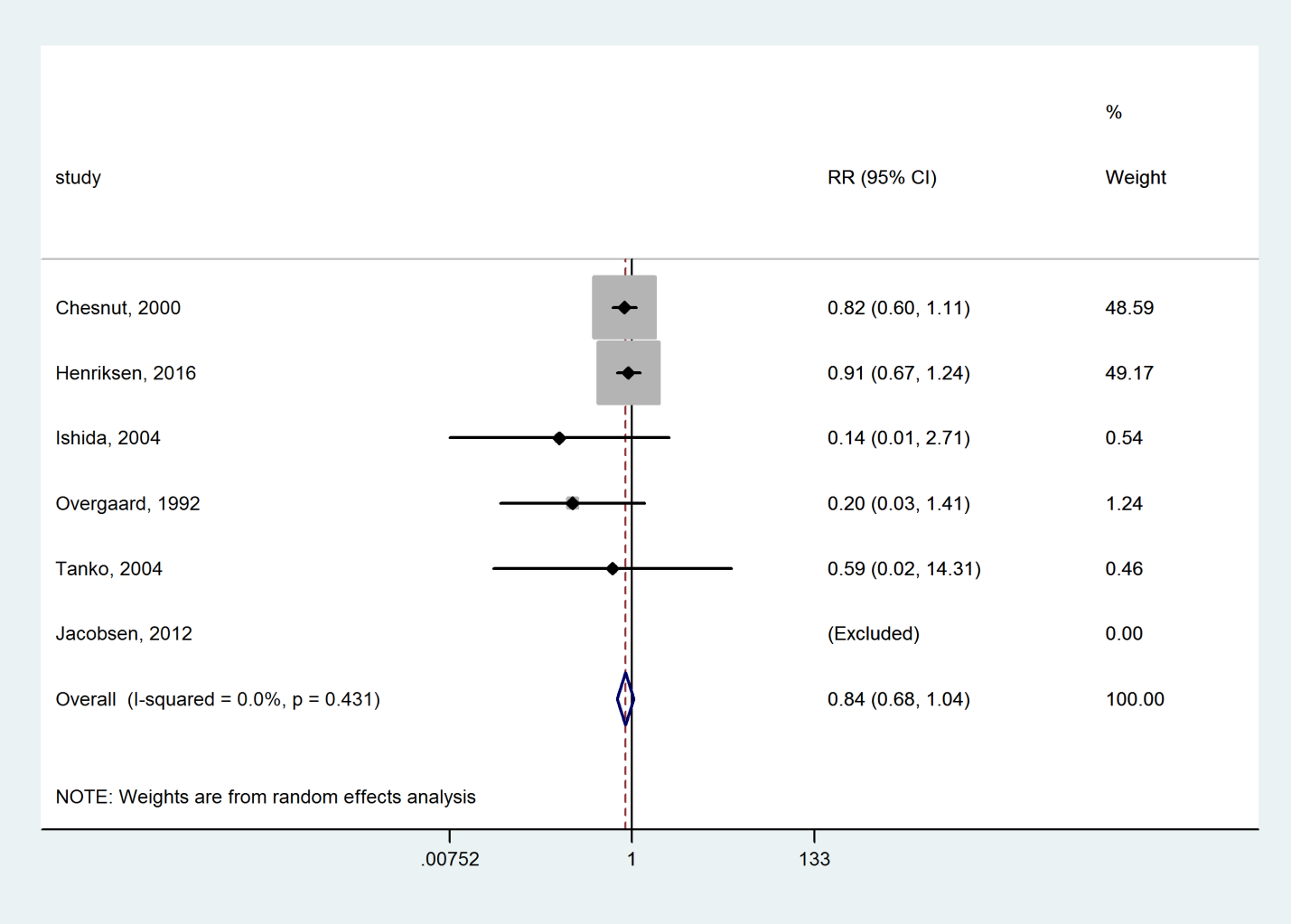
### Tibolone compared with Placebo



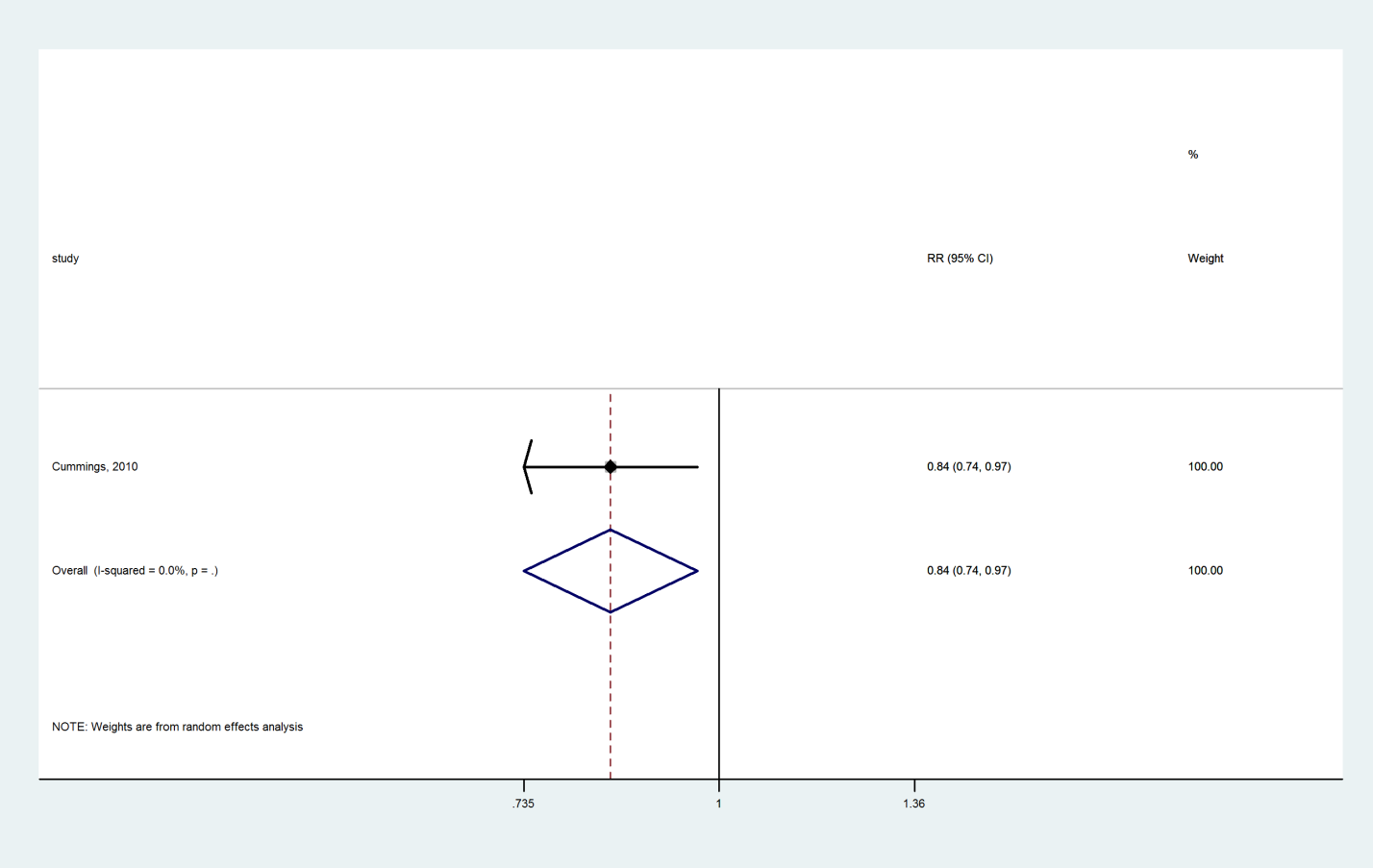
### Hormone therapy compared with Placebo



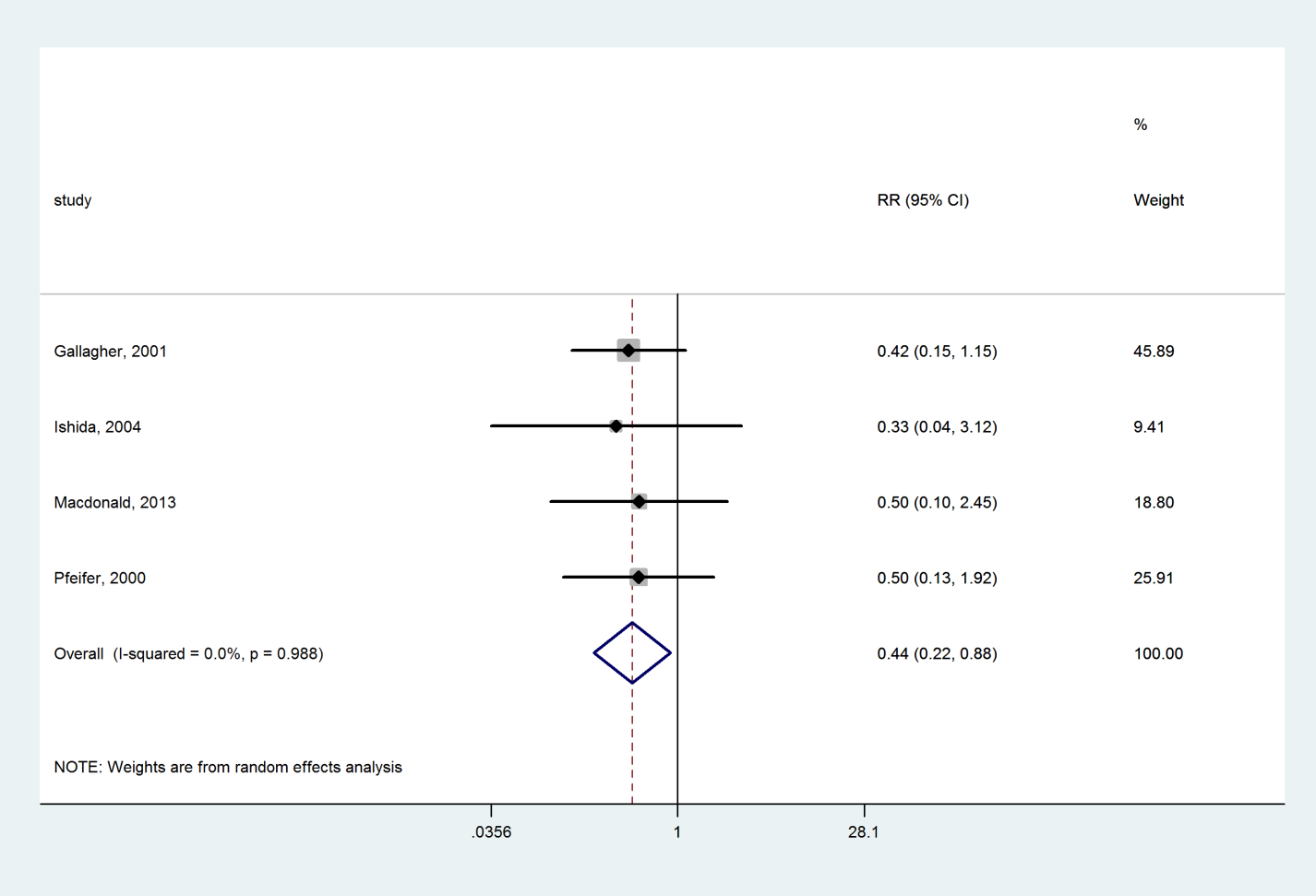
### Calcitonin compared with Placebo



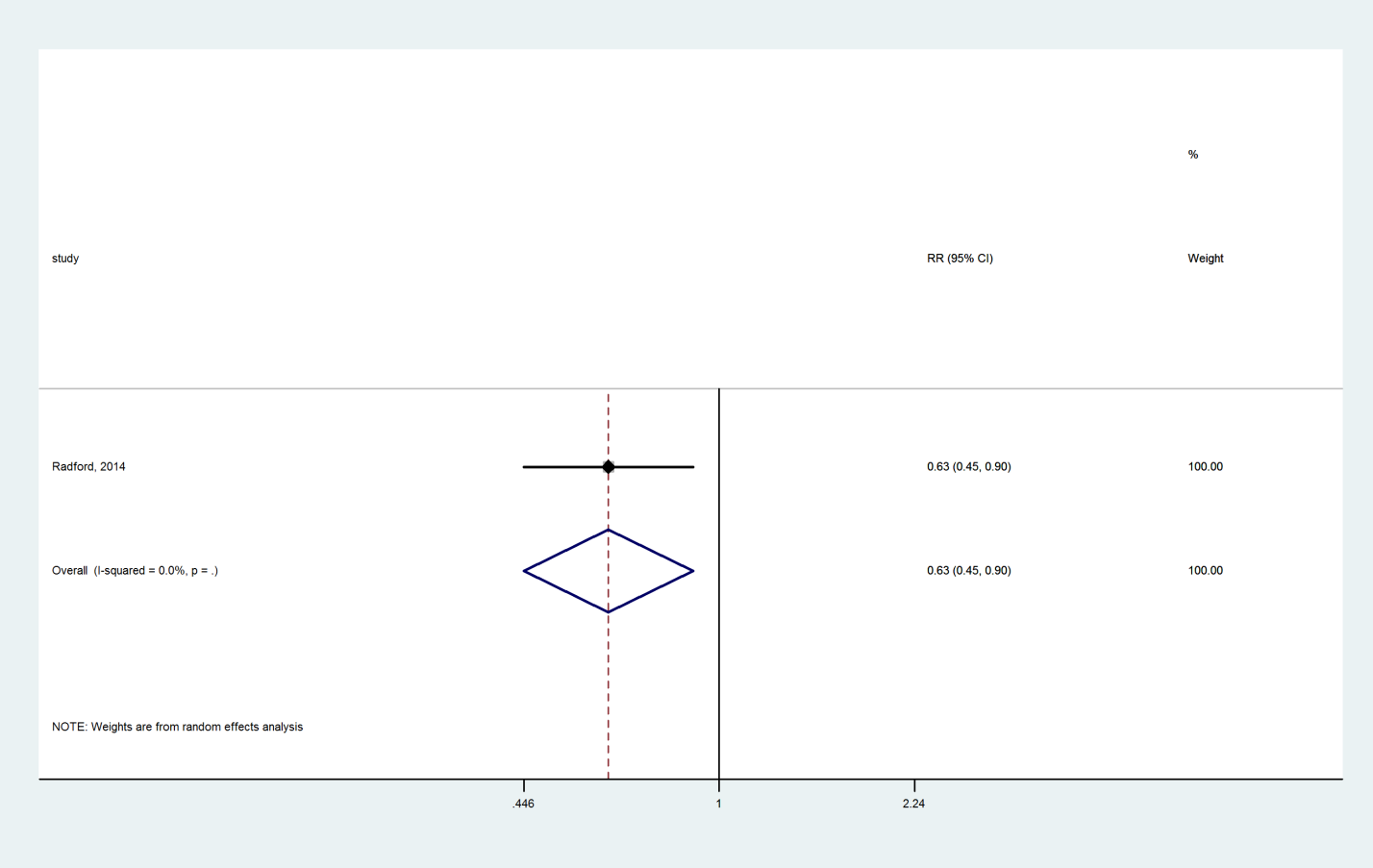
### Lasofoxifene compared with Placebo



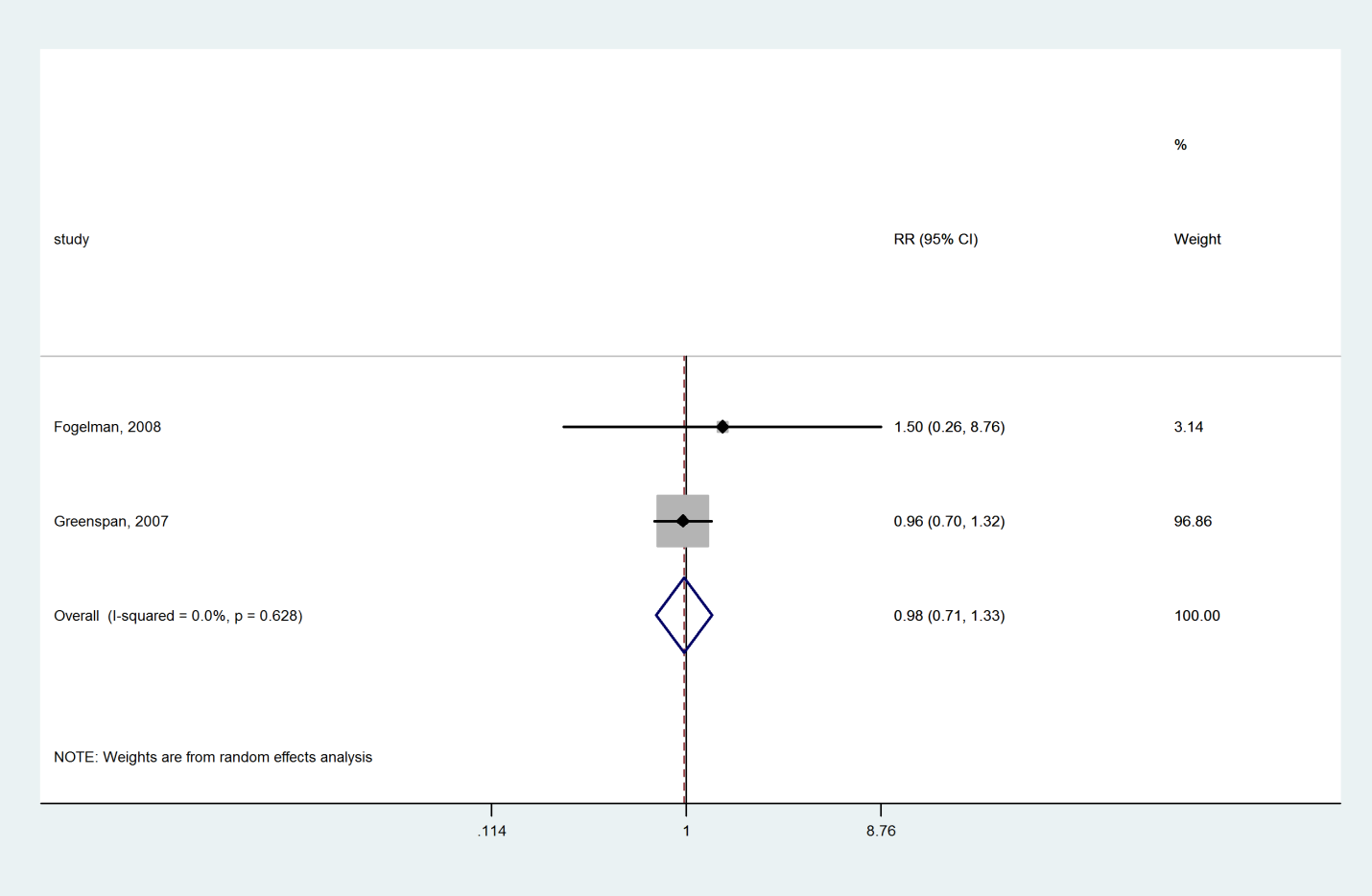
### Vitamin D compared with Placebo

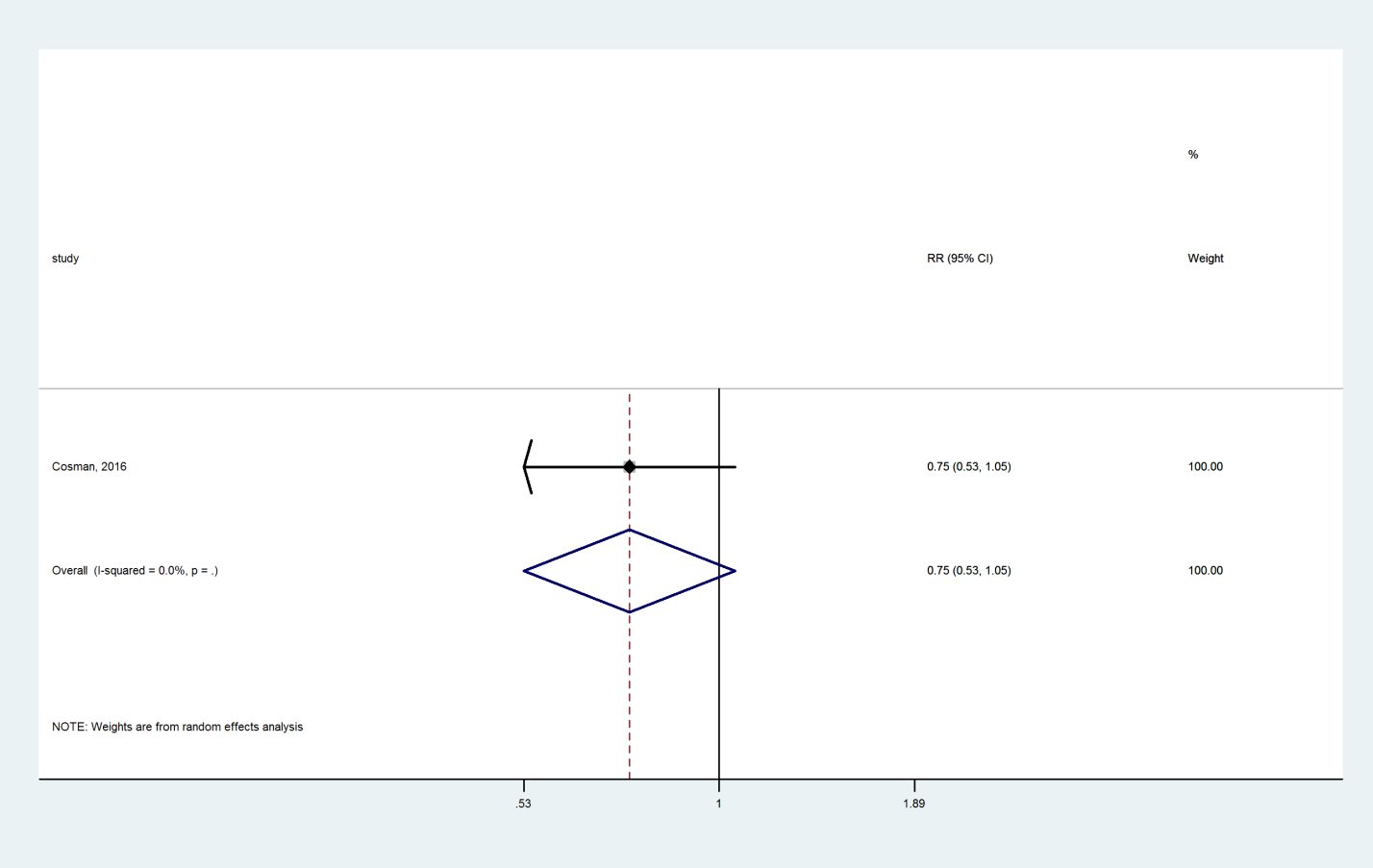


### Calcium compared with Placebo



### PTH 1-84 compared with Placebo

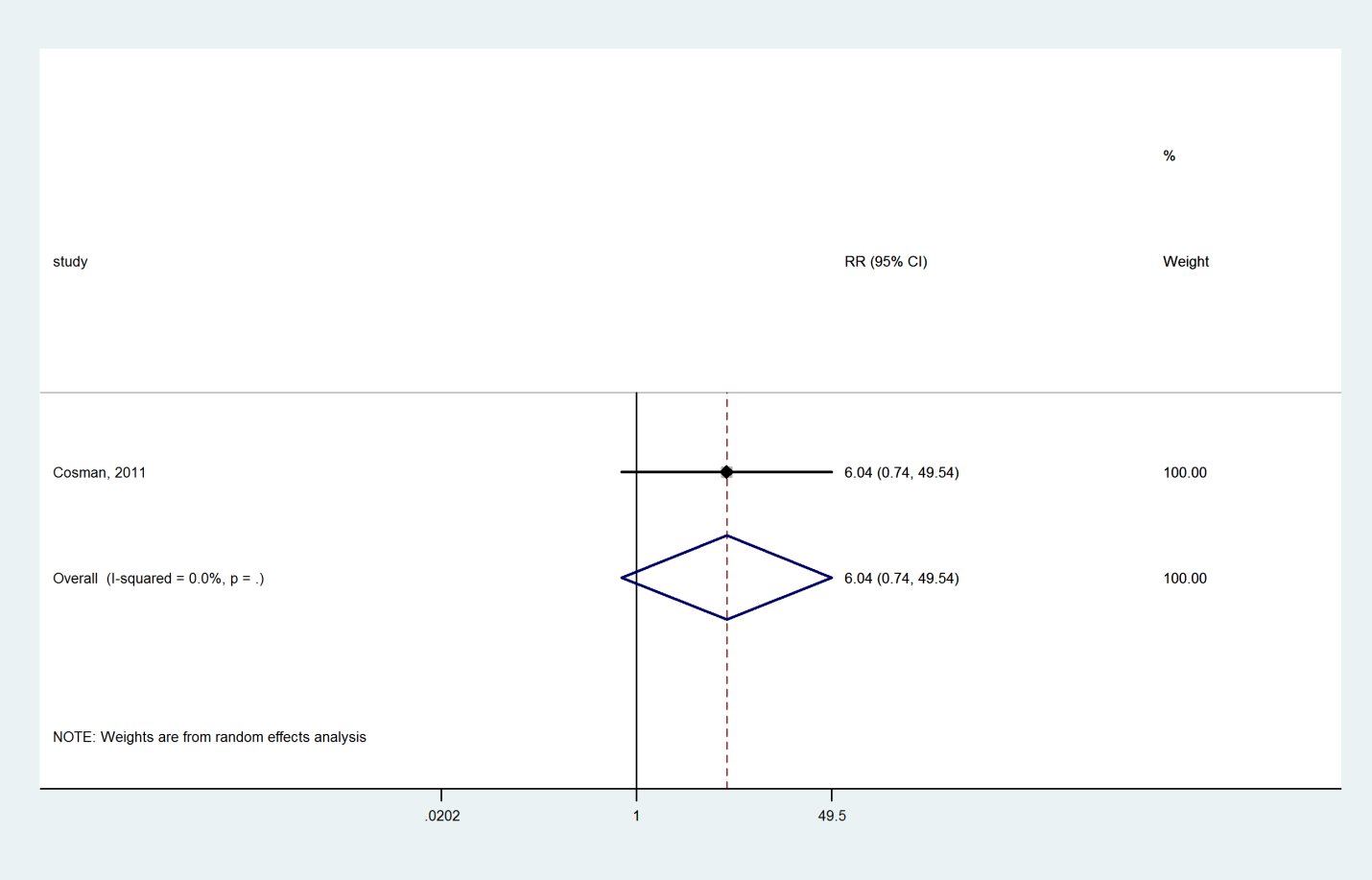


1. **Romosozumab compared with Placebo**

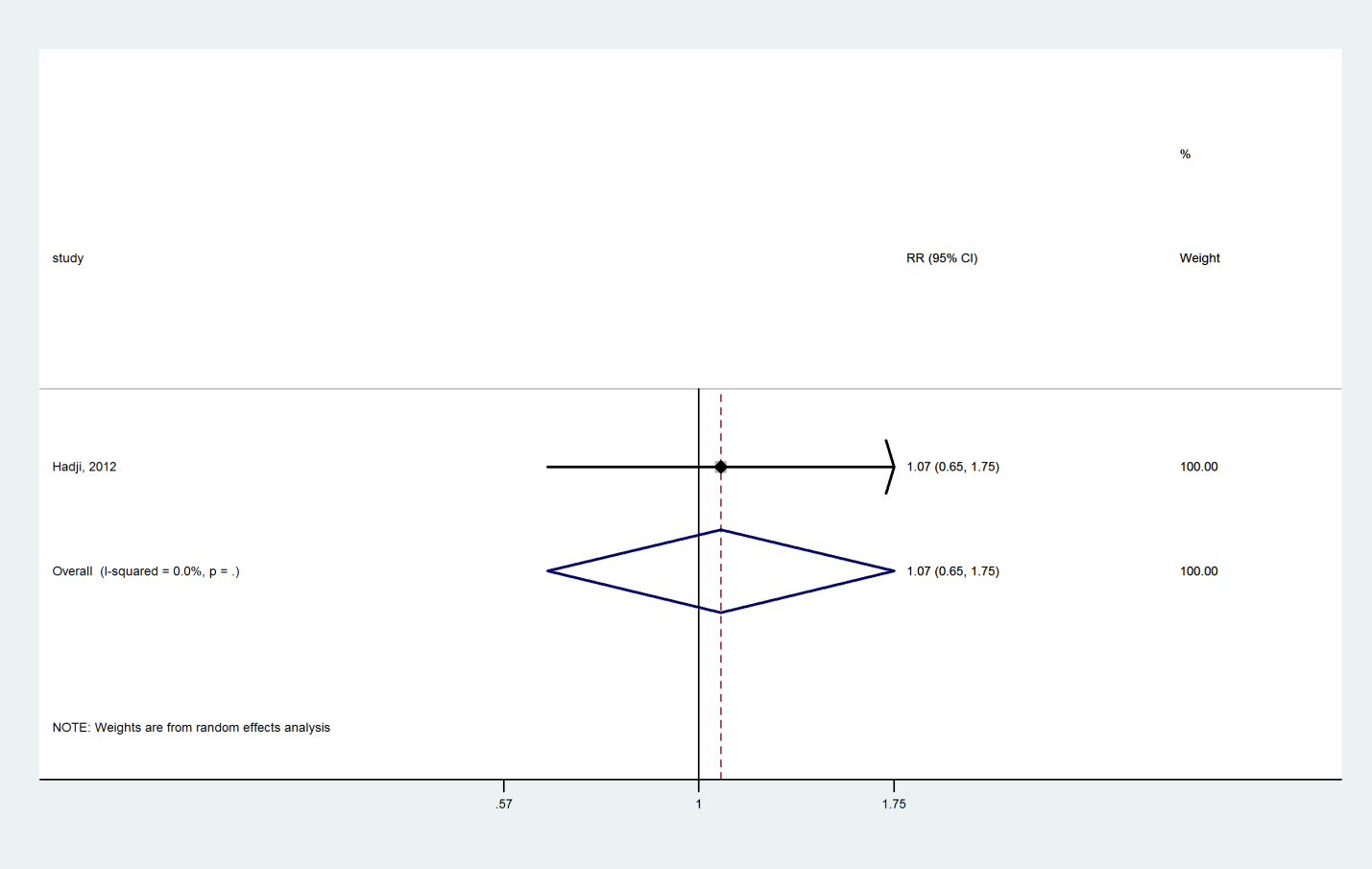
### Abaloparatide compared with Placebo



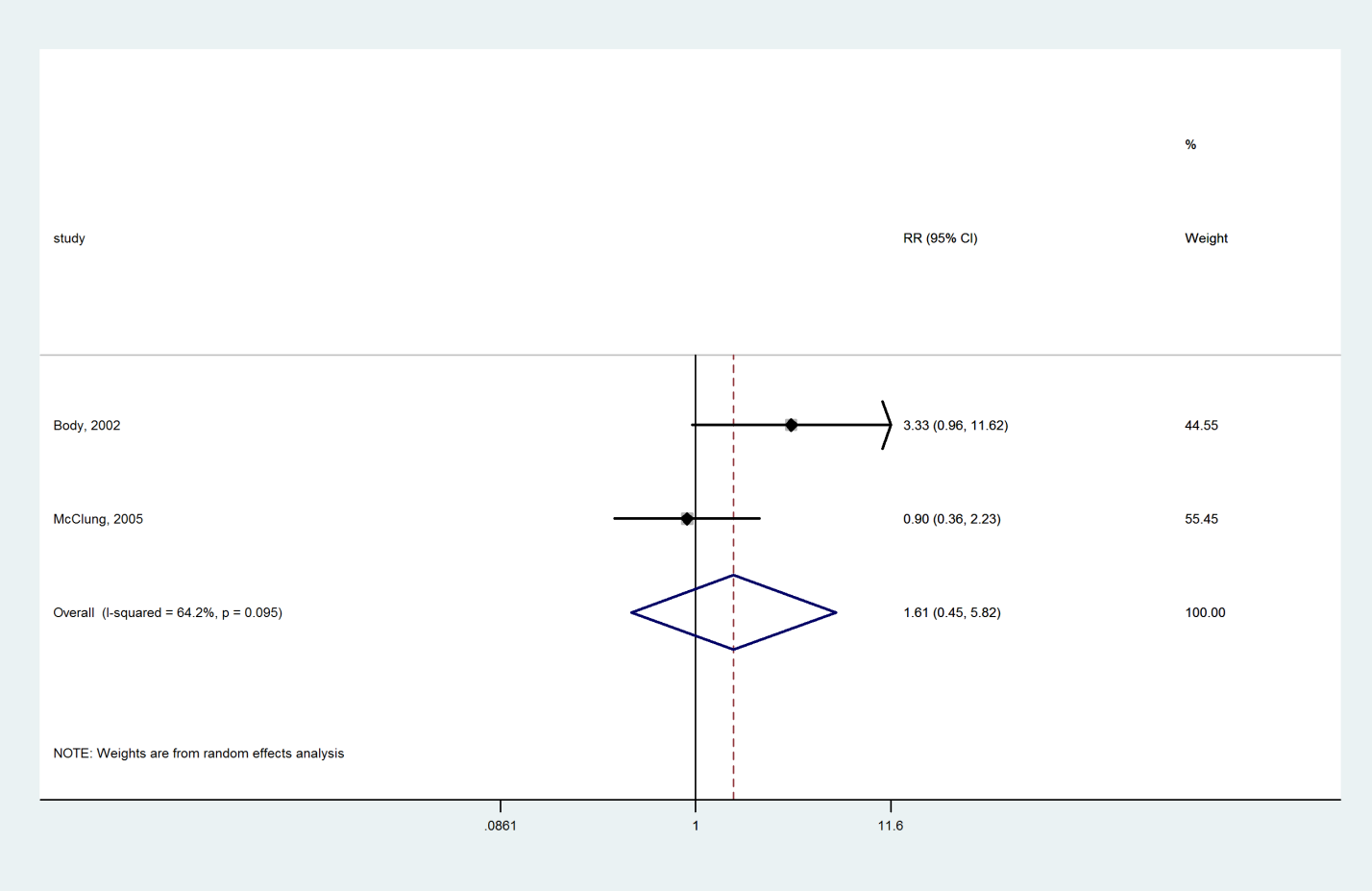
### Zoledronate compared with Teriparatide



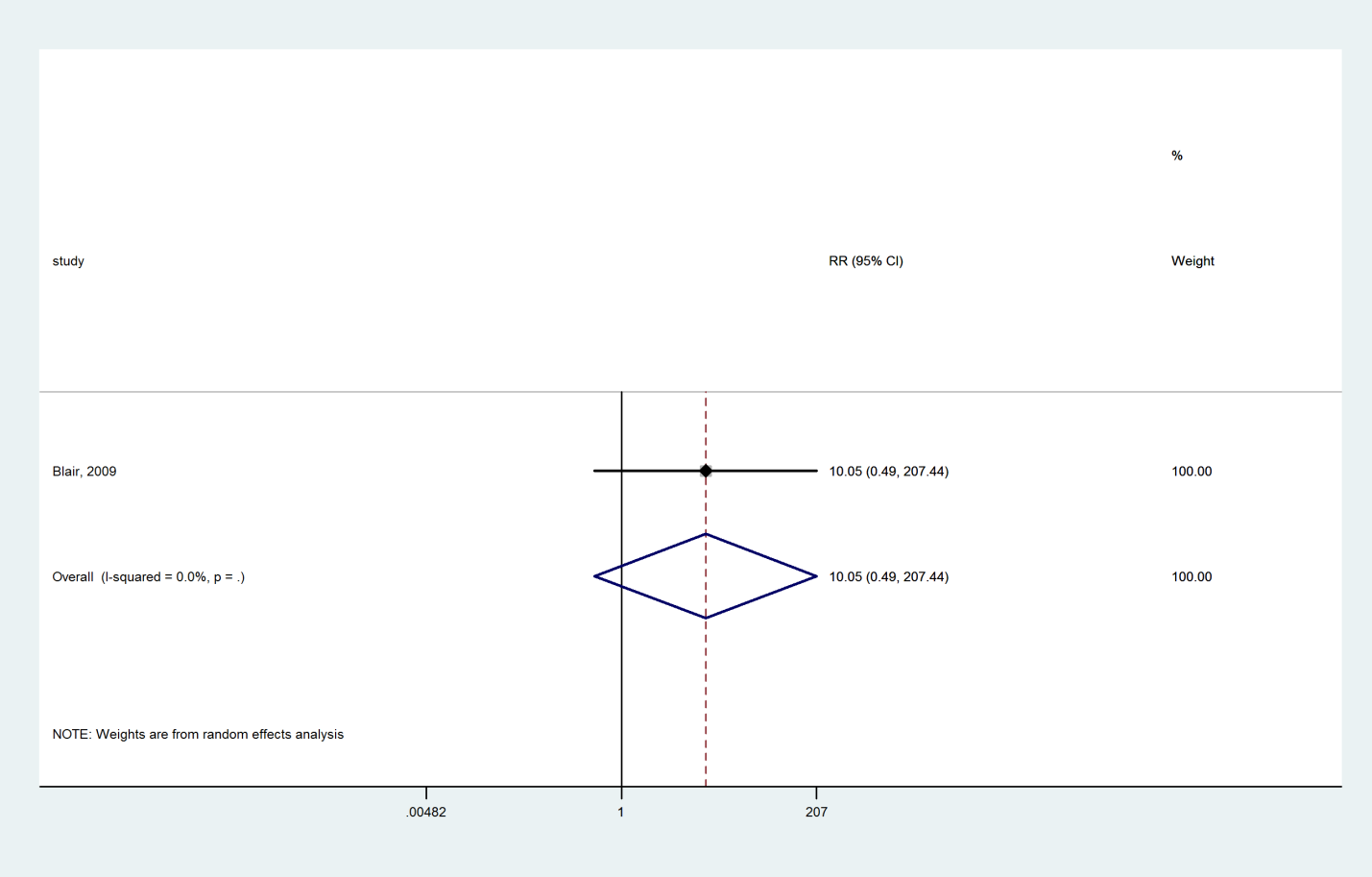
### Risedronate compared with Teriparatide



### Alendronate compared with Teriparatide



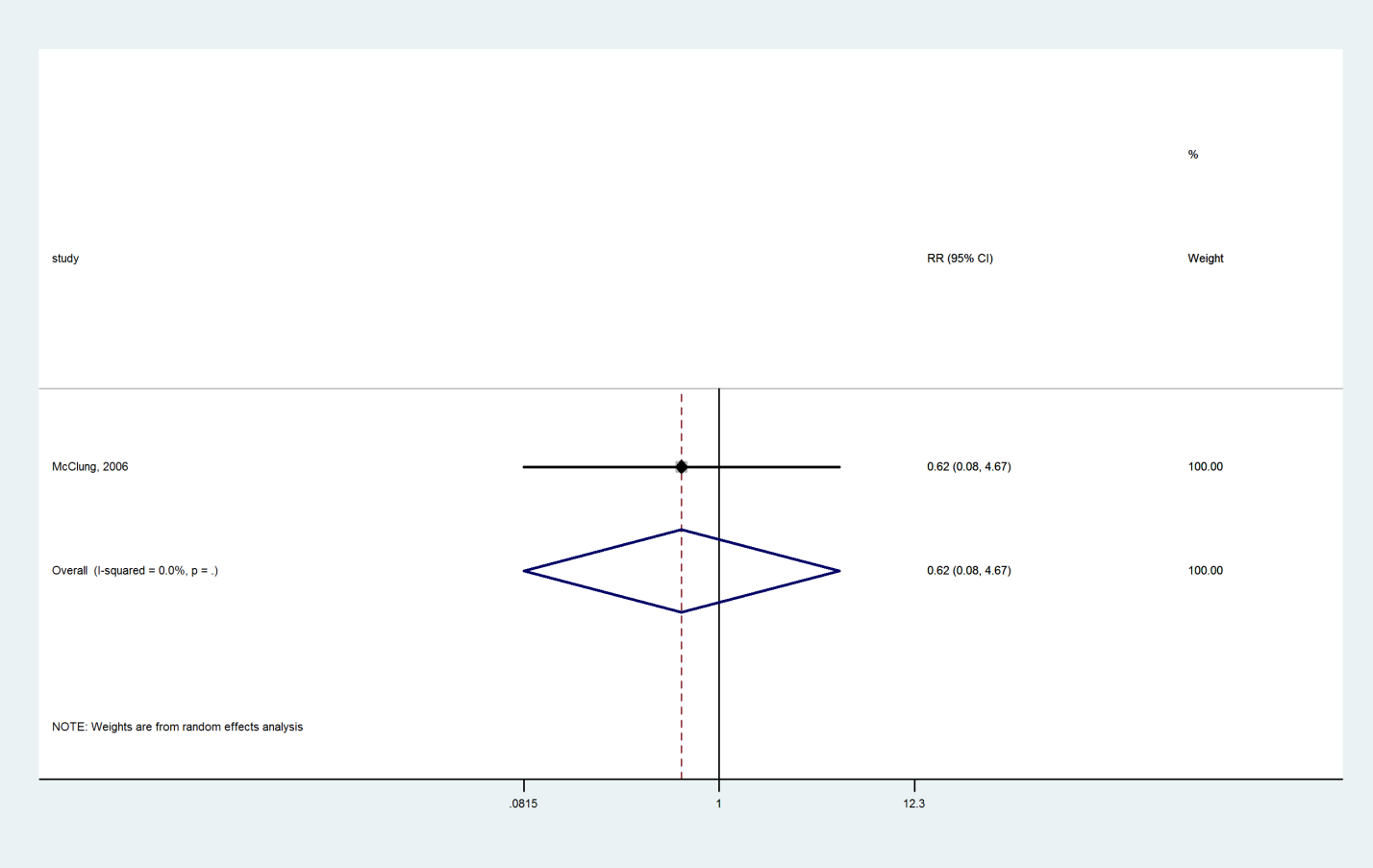
### Calcitonin compared with Teriparatide



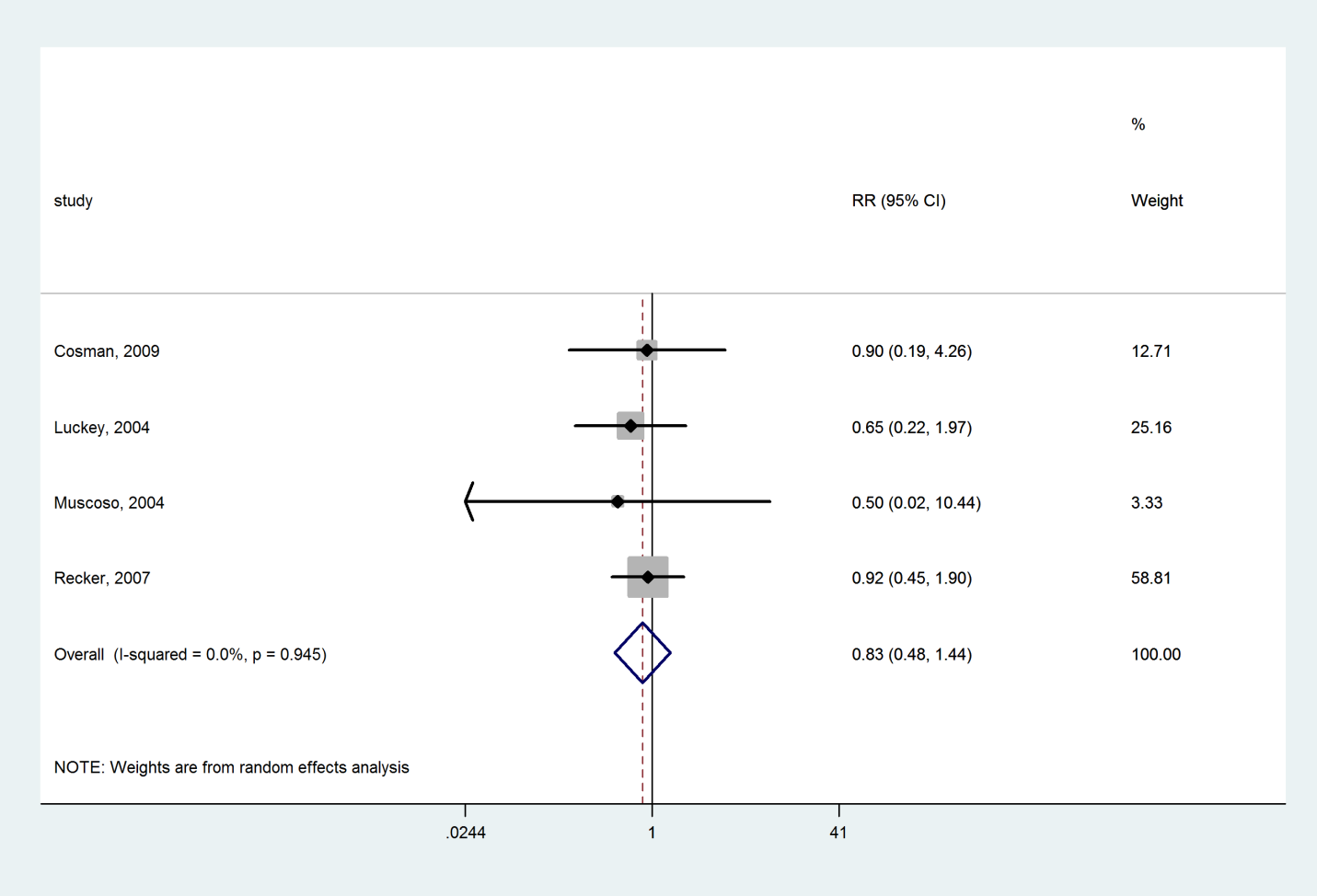
### Ibandronate compared with Denosumab

Y:\TES osteoporosis in women\SR in efficacy\6. Analysis\Direct and Indirect with STATA\2017-08\Direct\Graph_Nonvert_direct\trt7_trt3.wmf

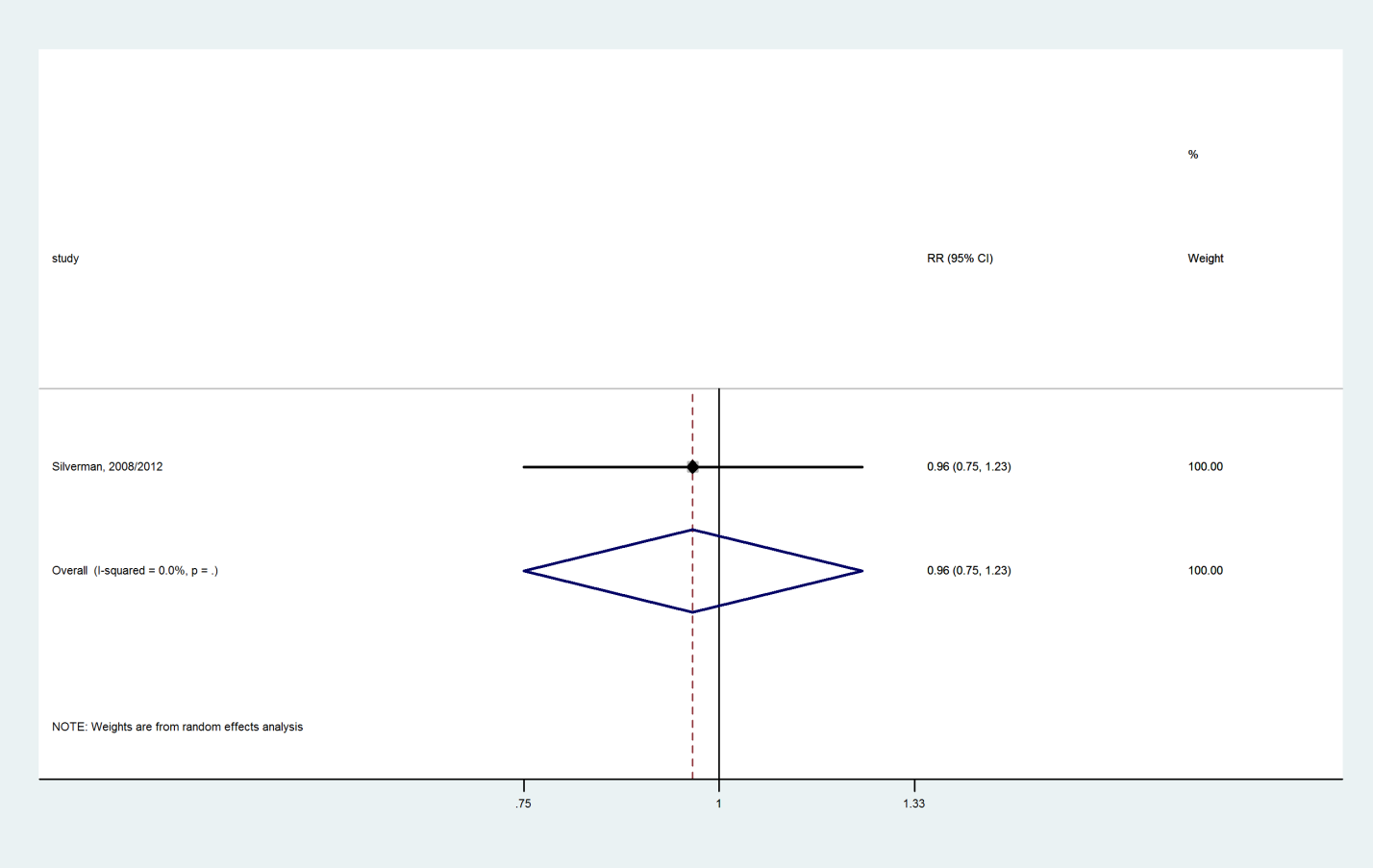
### Alendronate compared with Denosumab



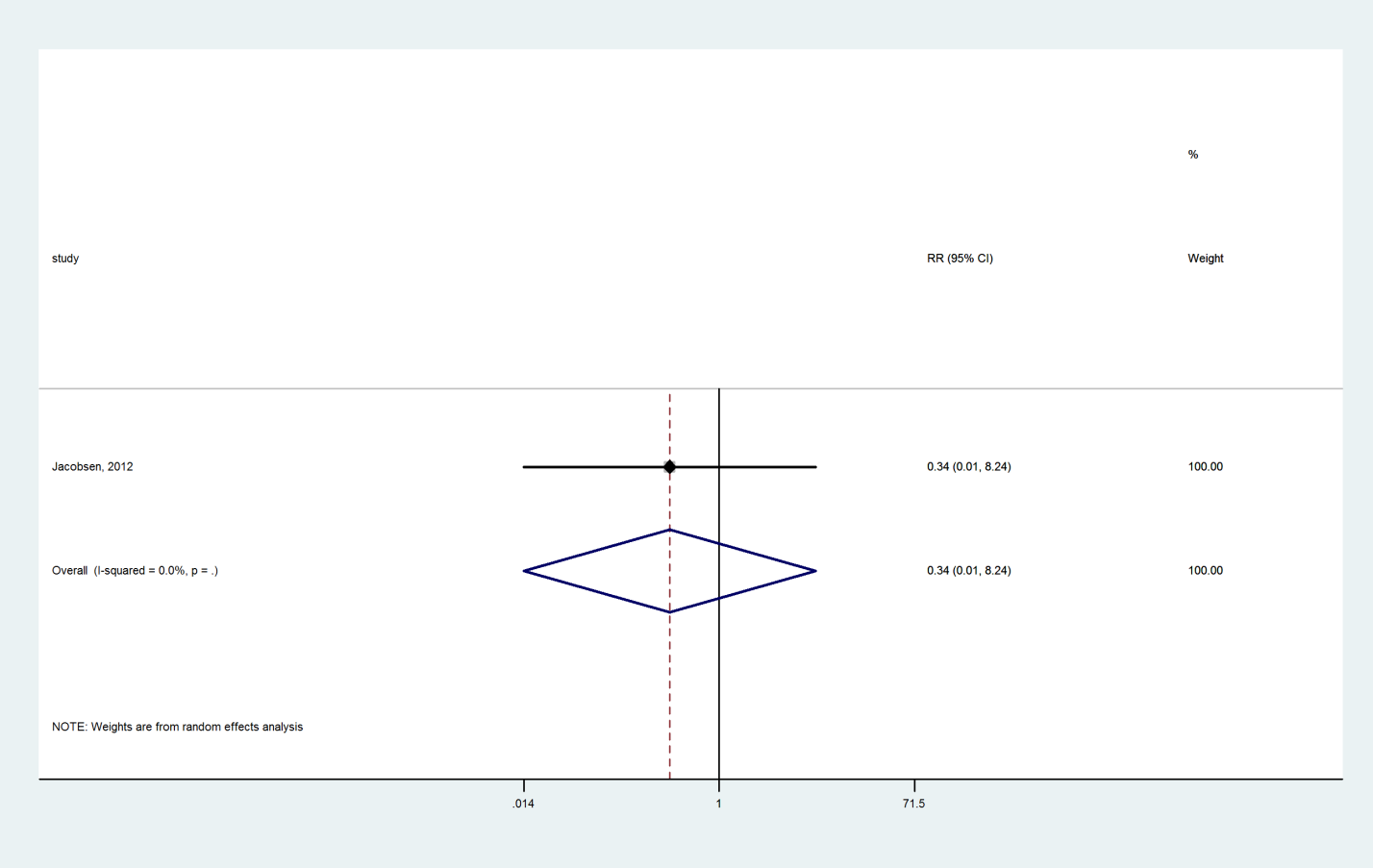
### Alendronate compared with Raloxifene



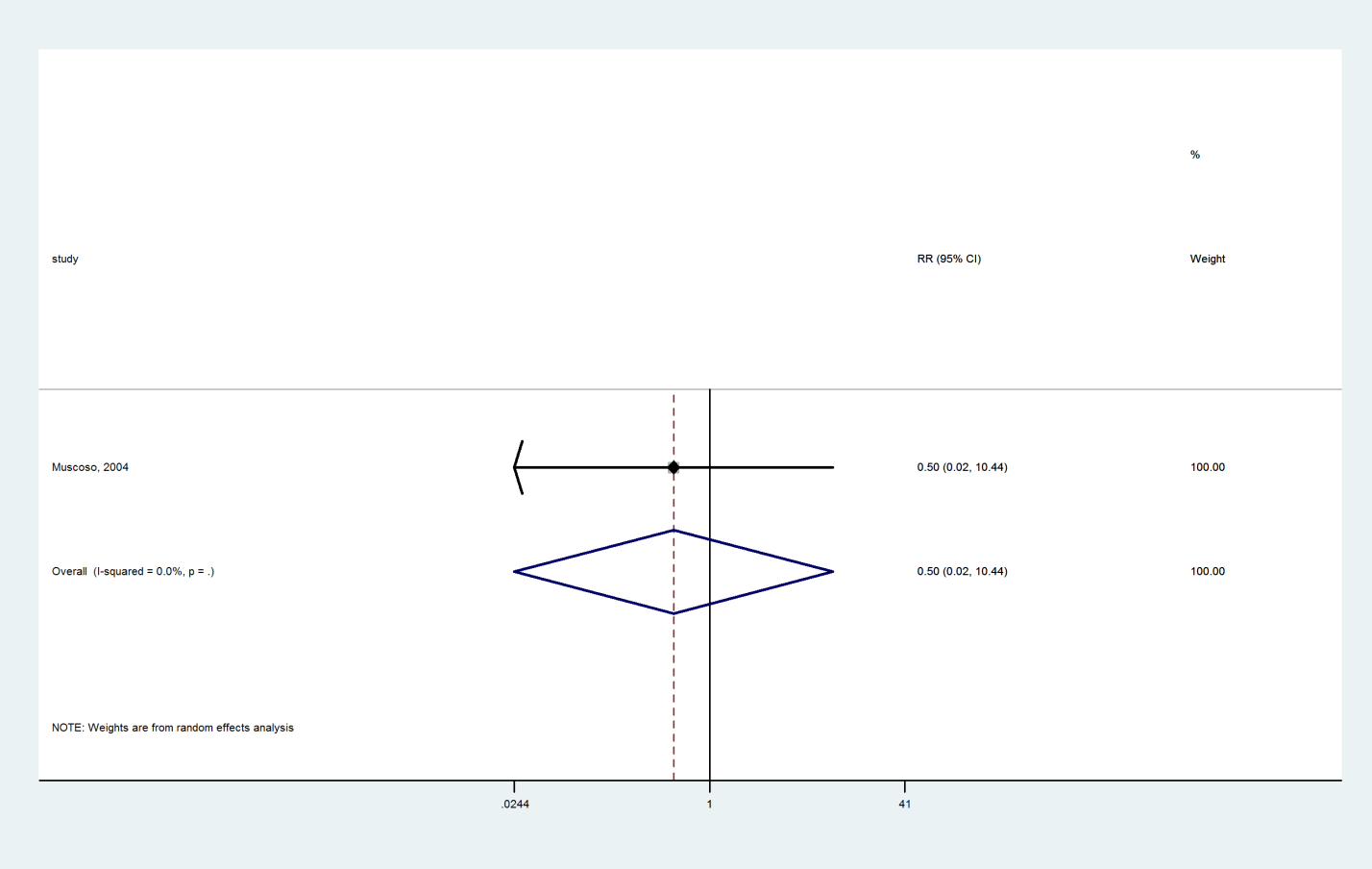
### Bazedoxifene compared with Raloxifene



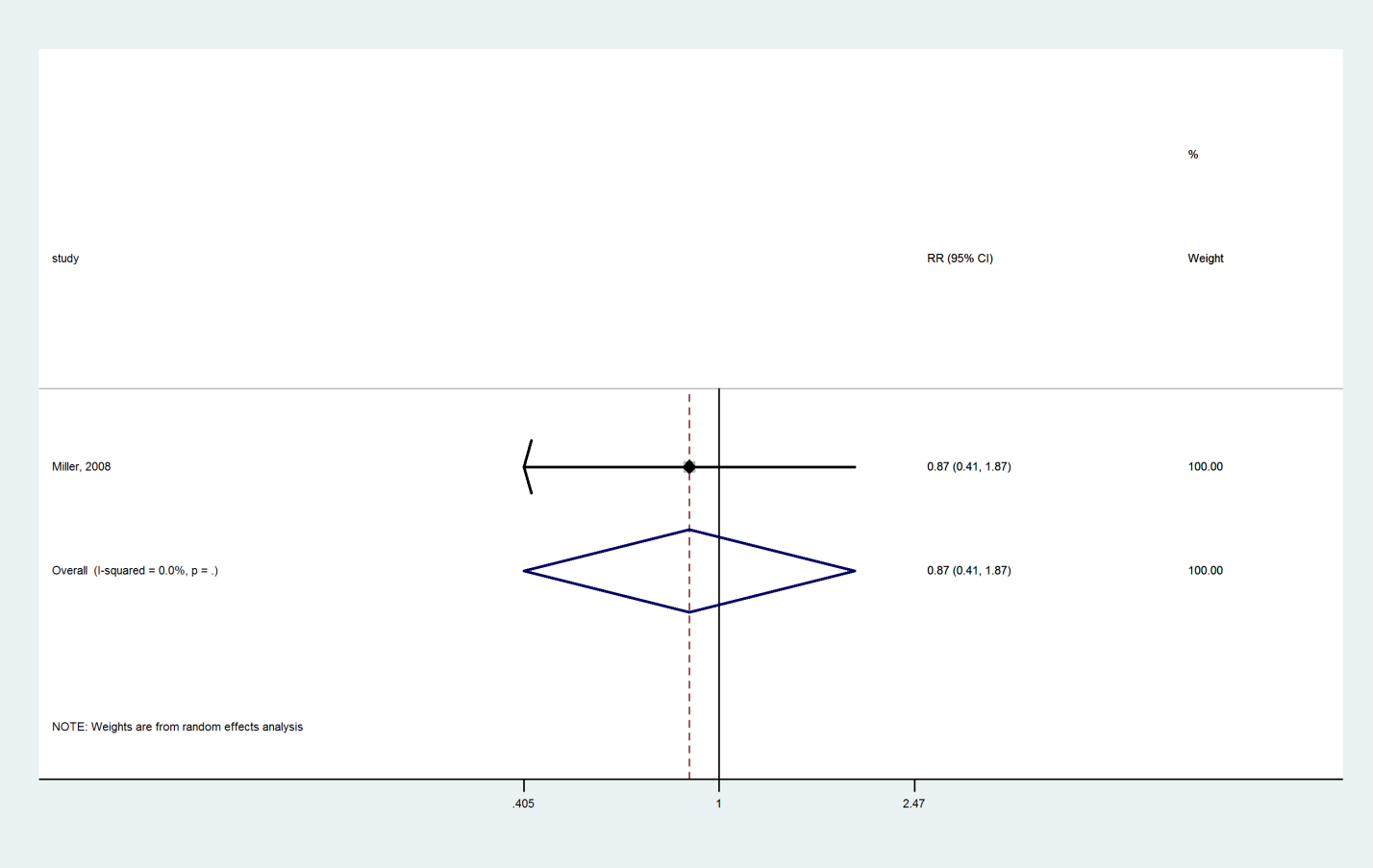
### Calcitonin compared with Raloxifene



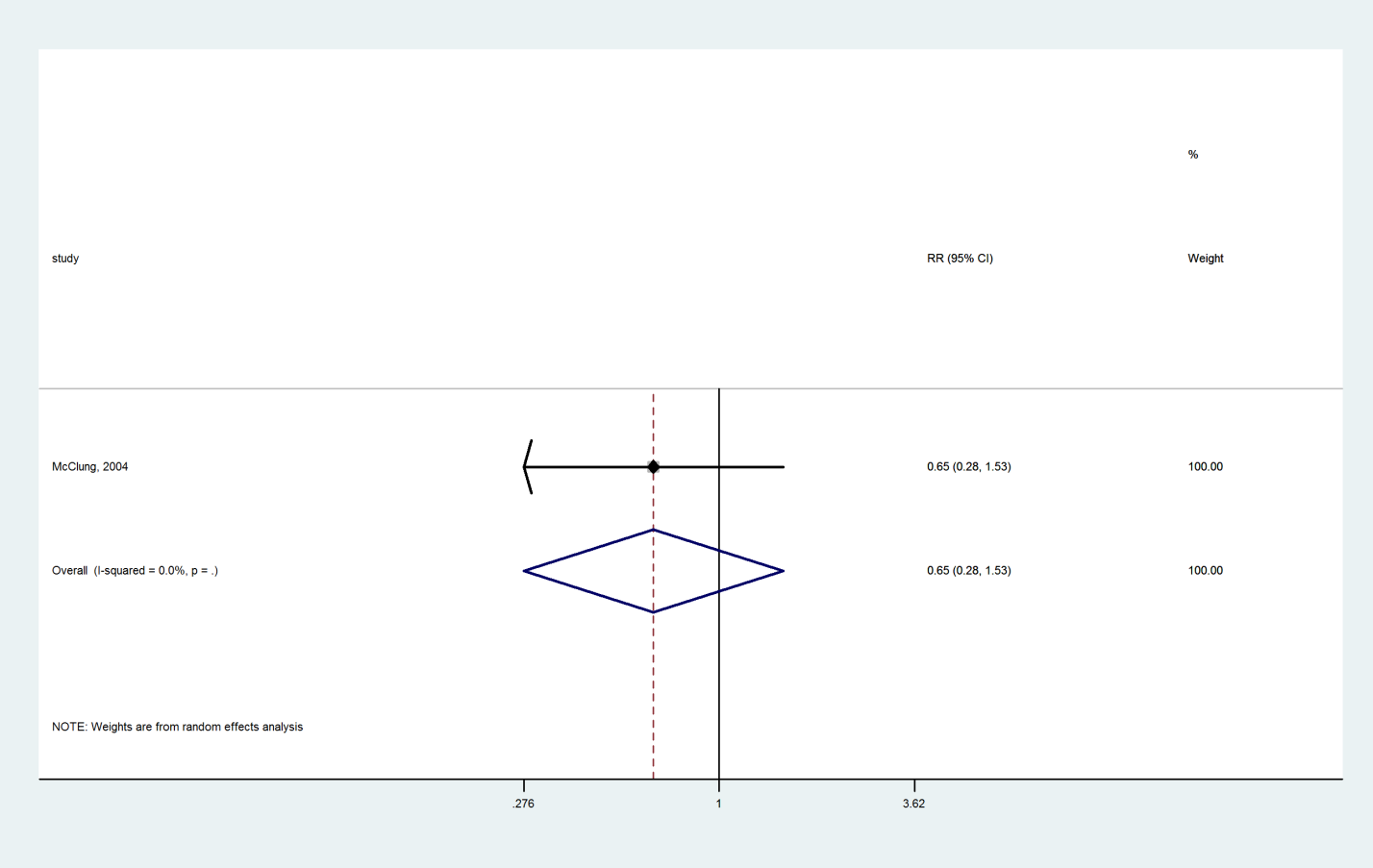
### Alendronate compared with Risedronate



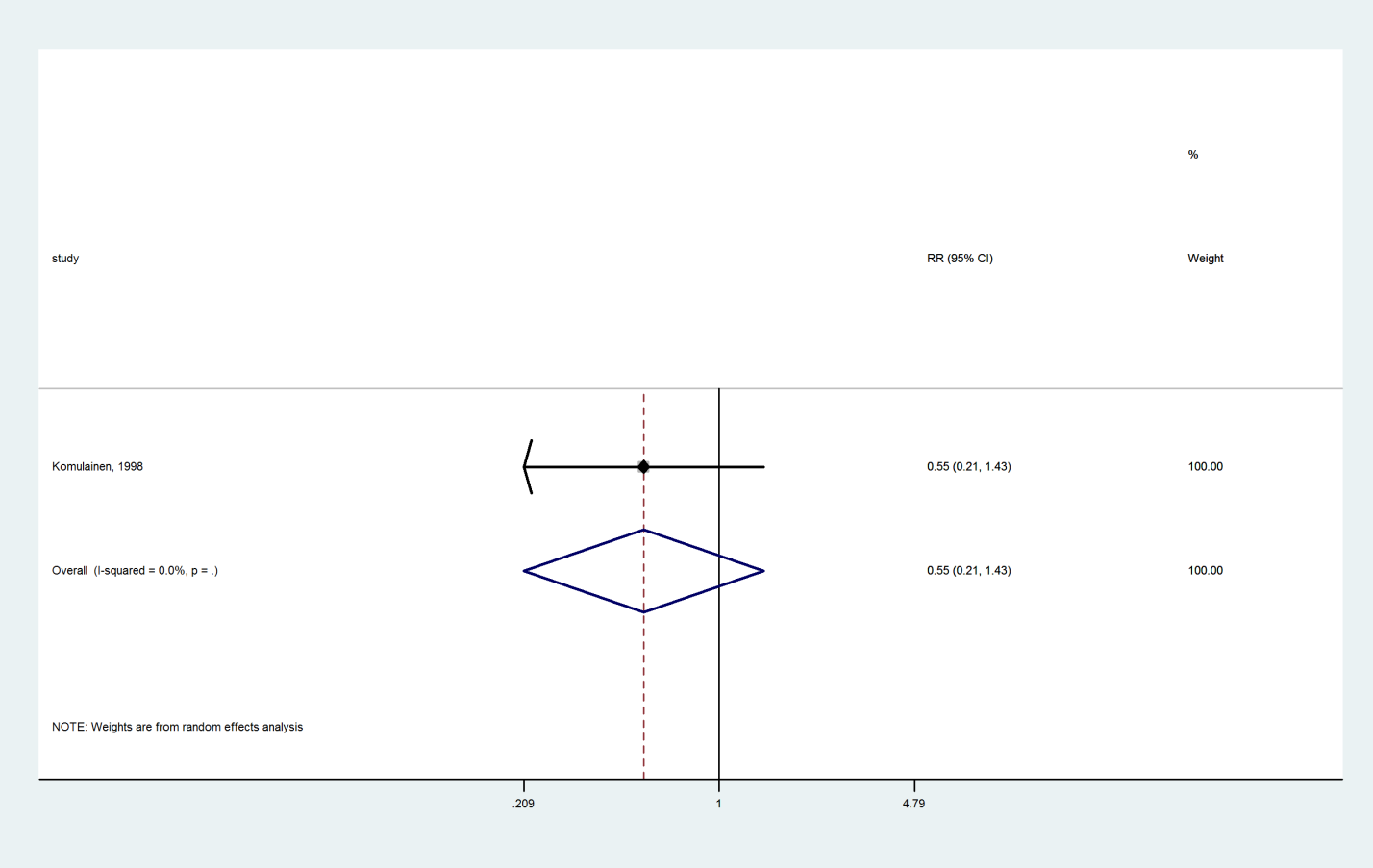
### Alendronate compared with Ibandronate



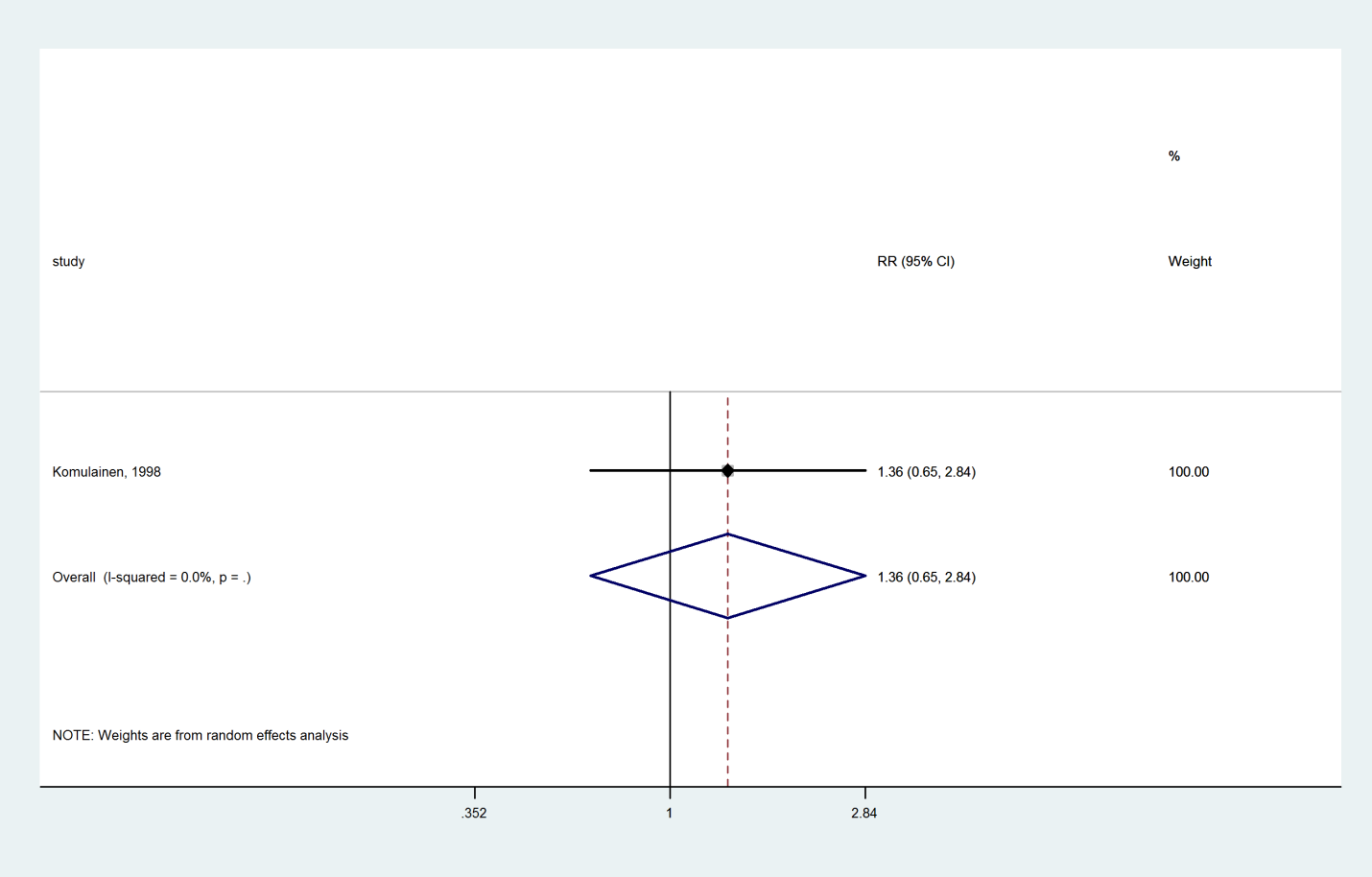
### Hormone therapy compared with Alendronate



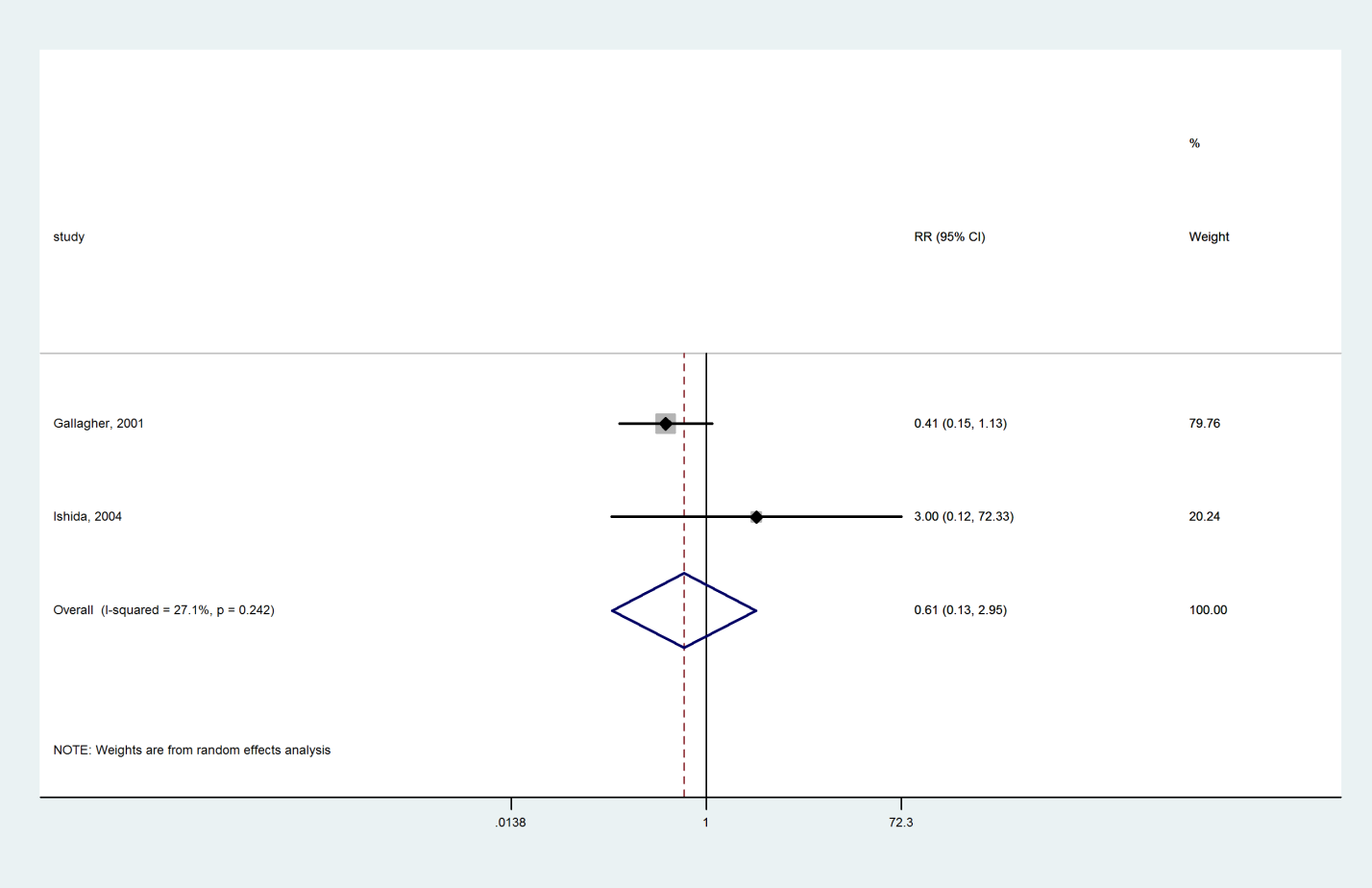
### Hormone therapy compared with Vitamin D+Calcium



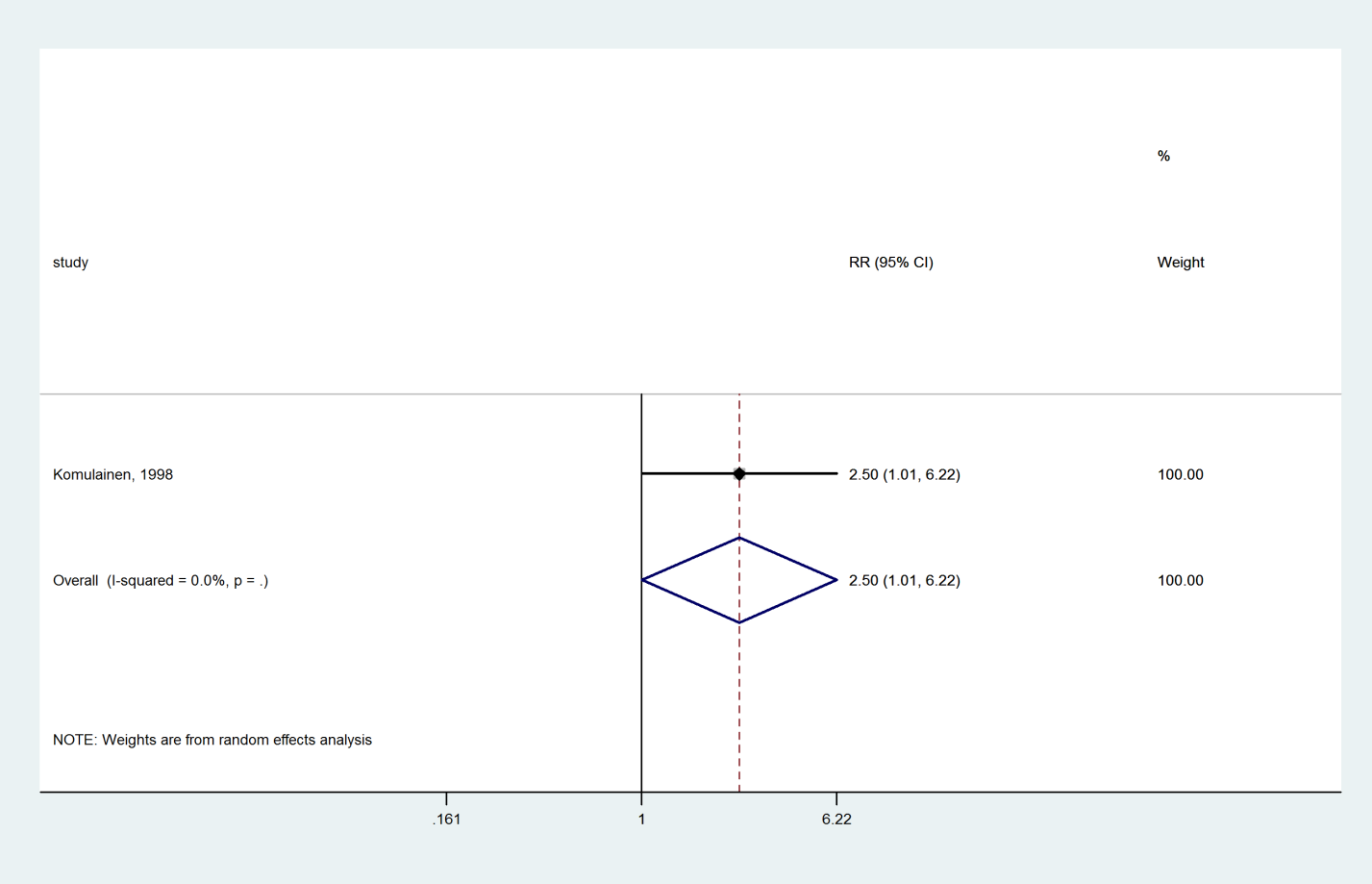
### Calcium compared with Vitamin D+Calcium



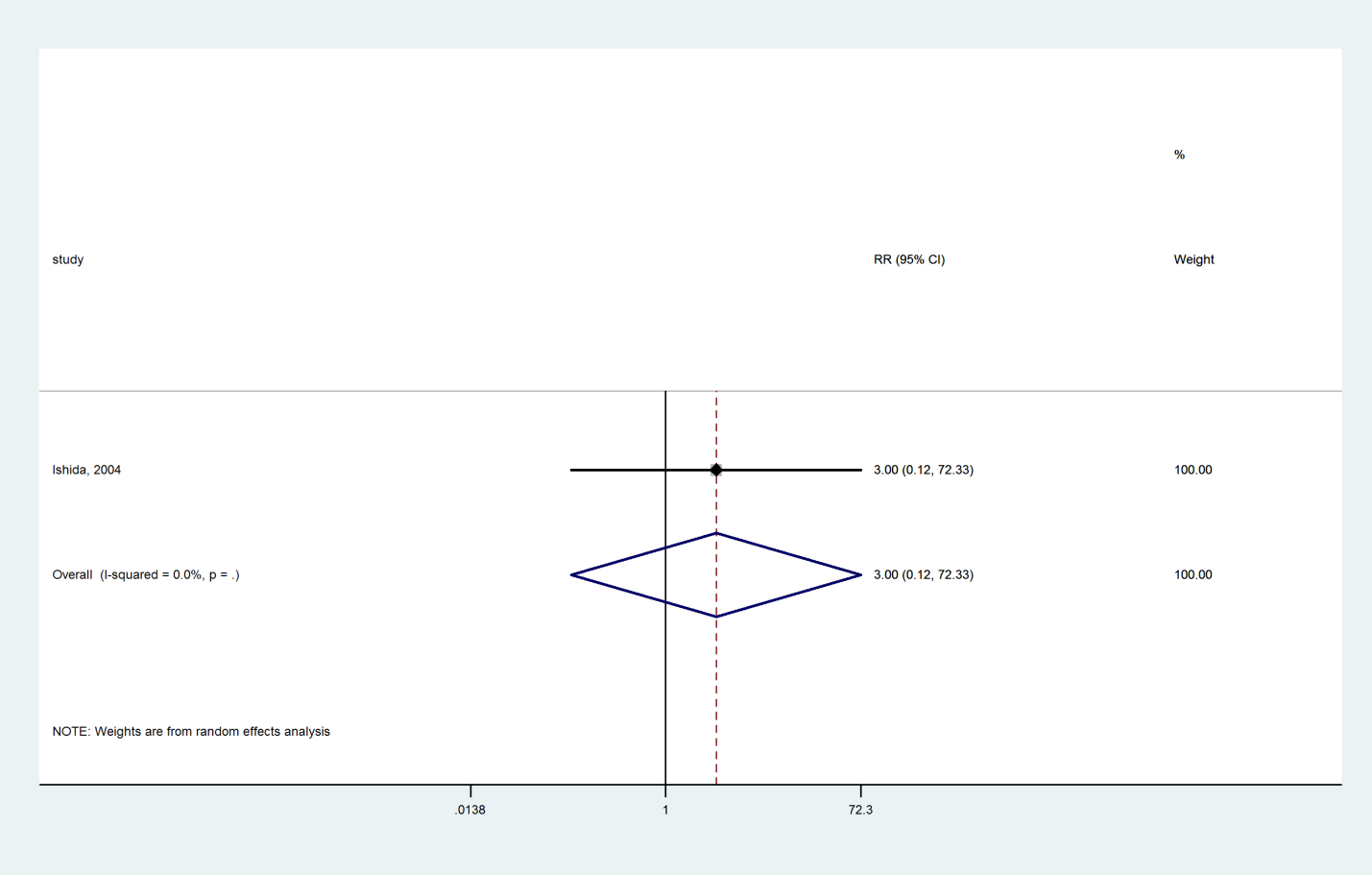
### Vitamin D compared with Hormone therapy



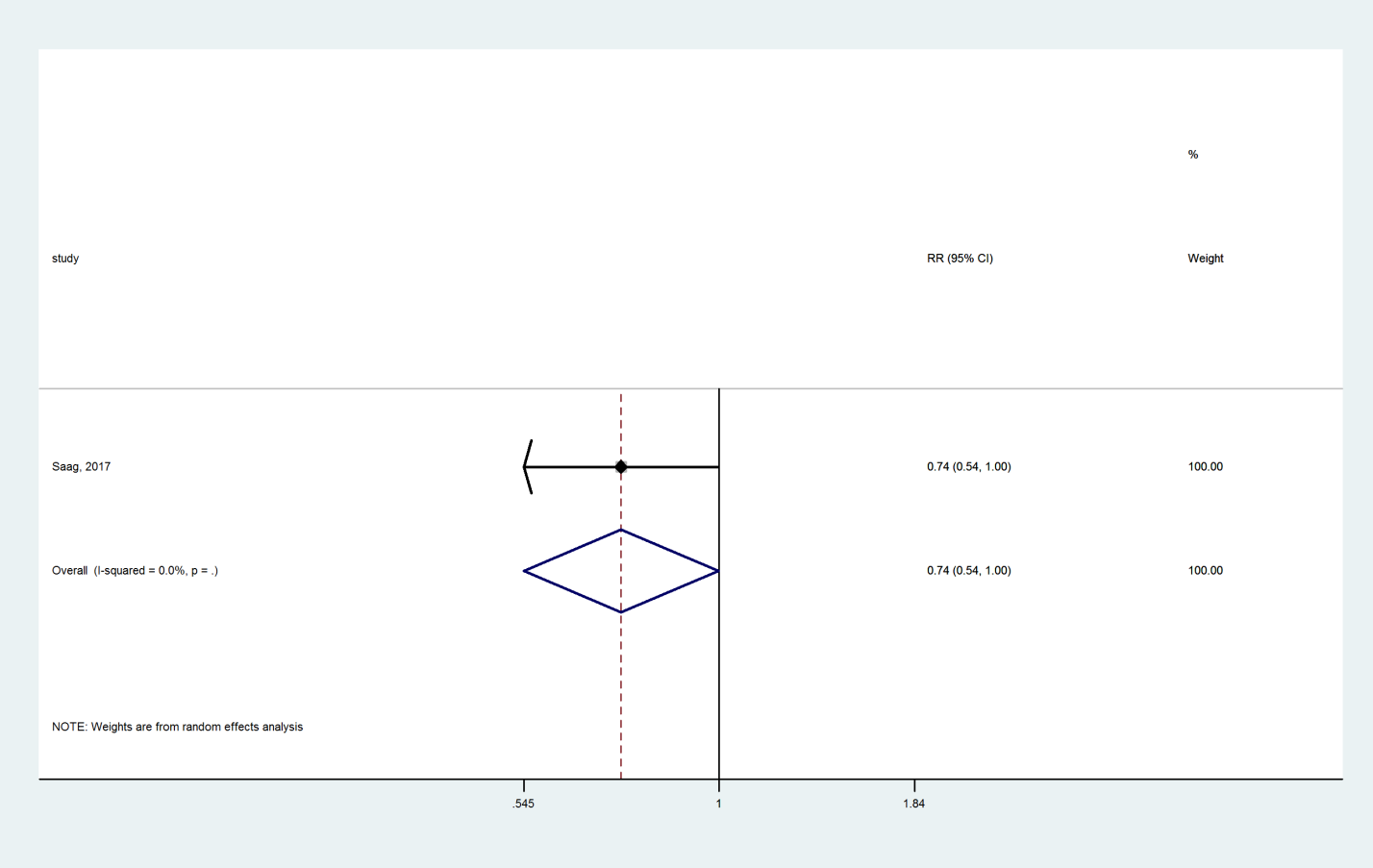
### Calcium compared with Hormone therapy



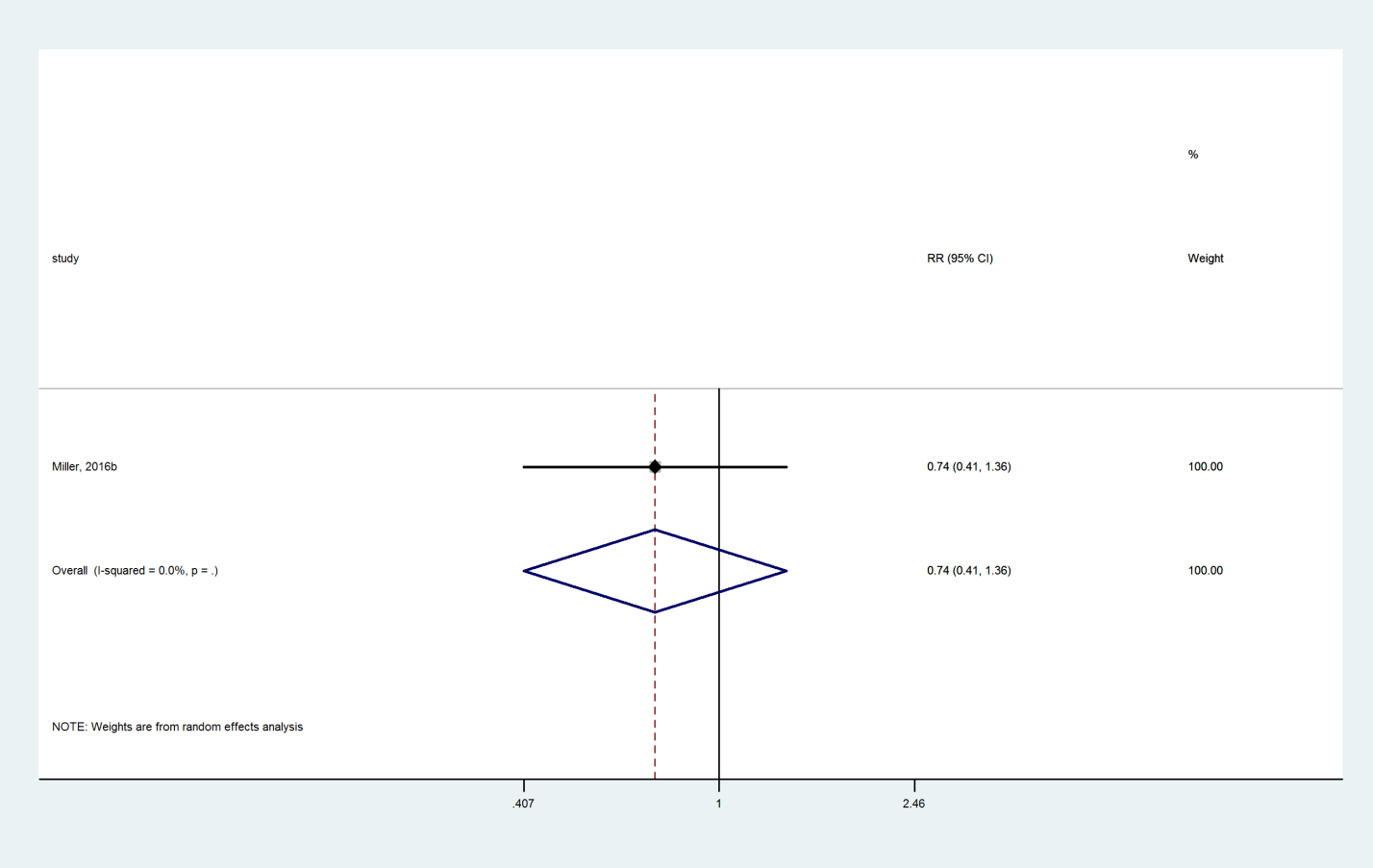
### Vitamin D compared with Calcitonin



### Romosozumab compared with Alendronate

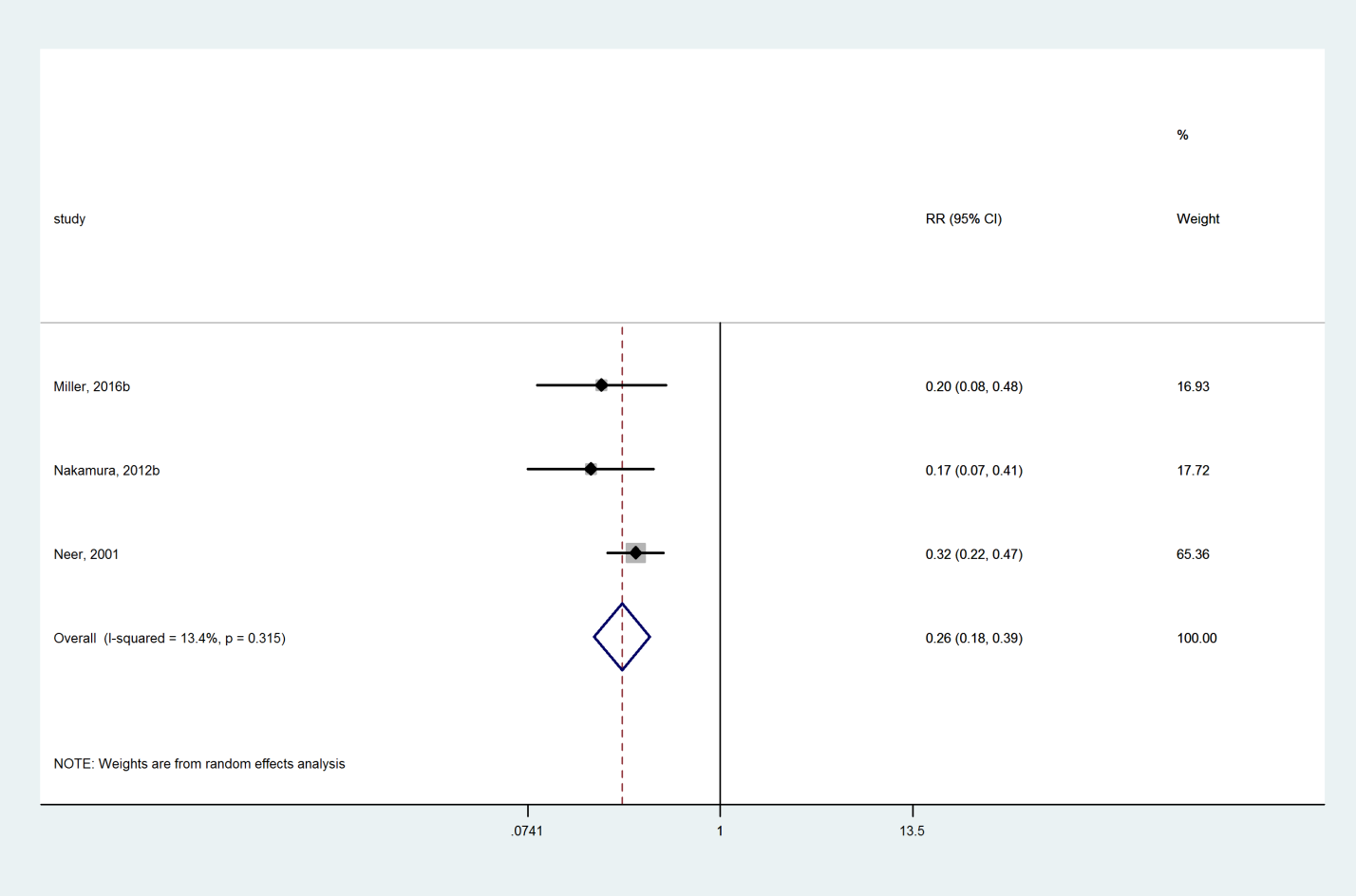


### Abaloparatide compared with Teriparatide

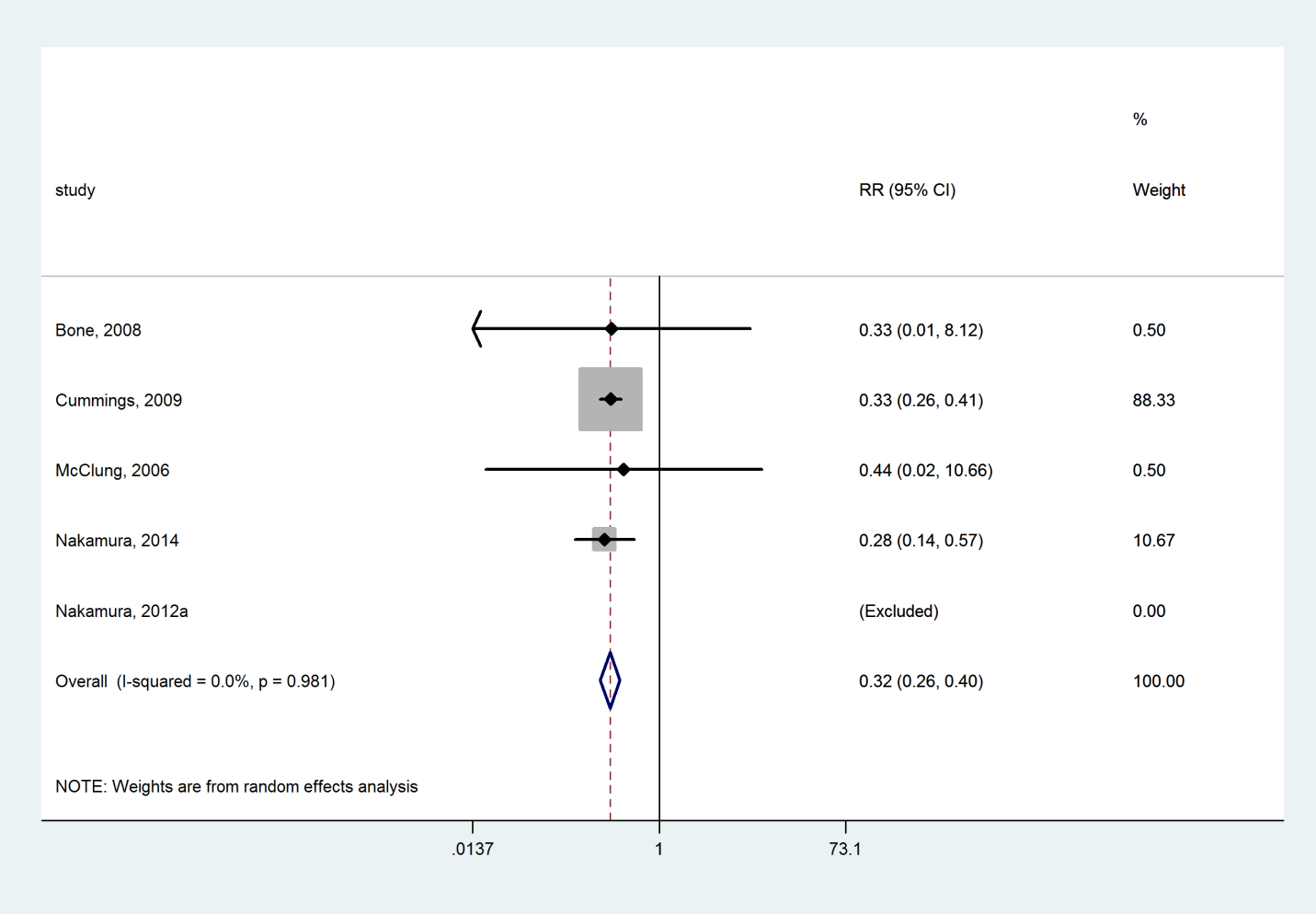


## Vertebral Fracture

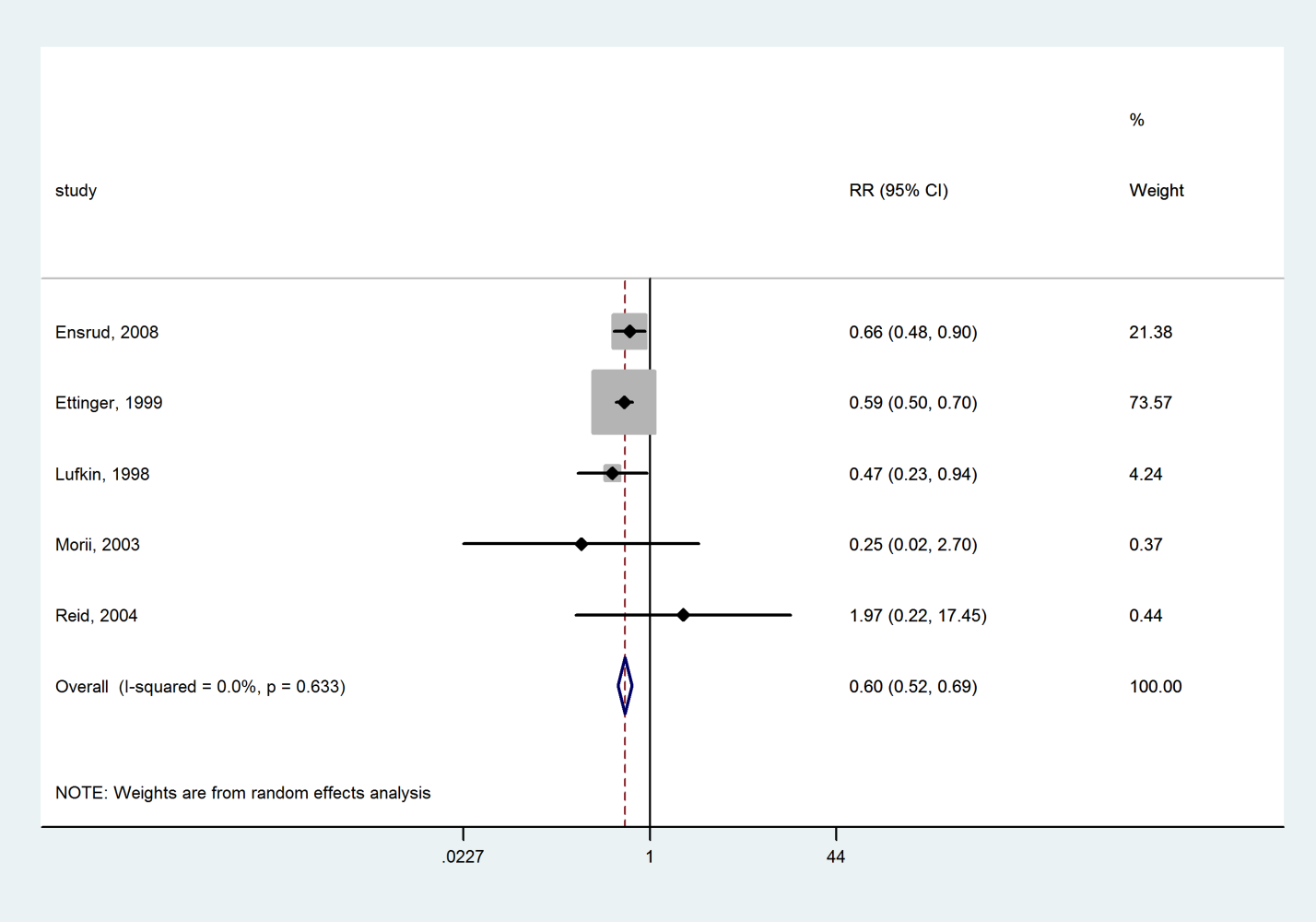
### Teriparatide compared with Placebo



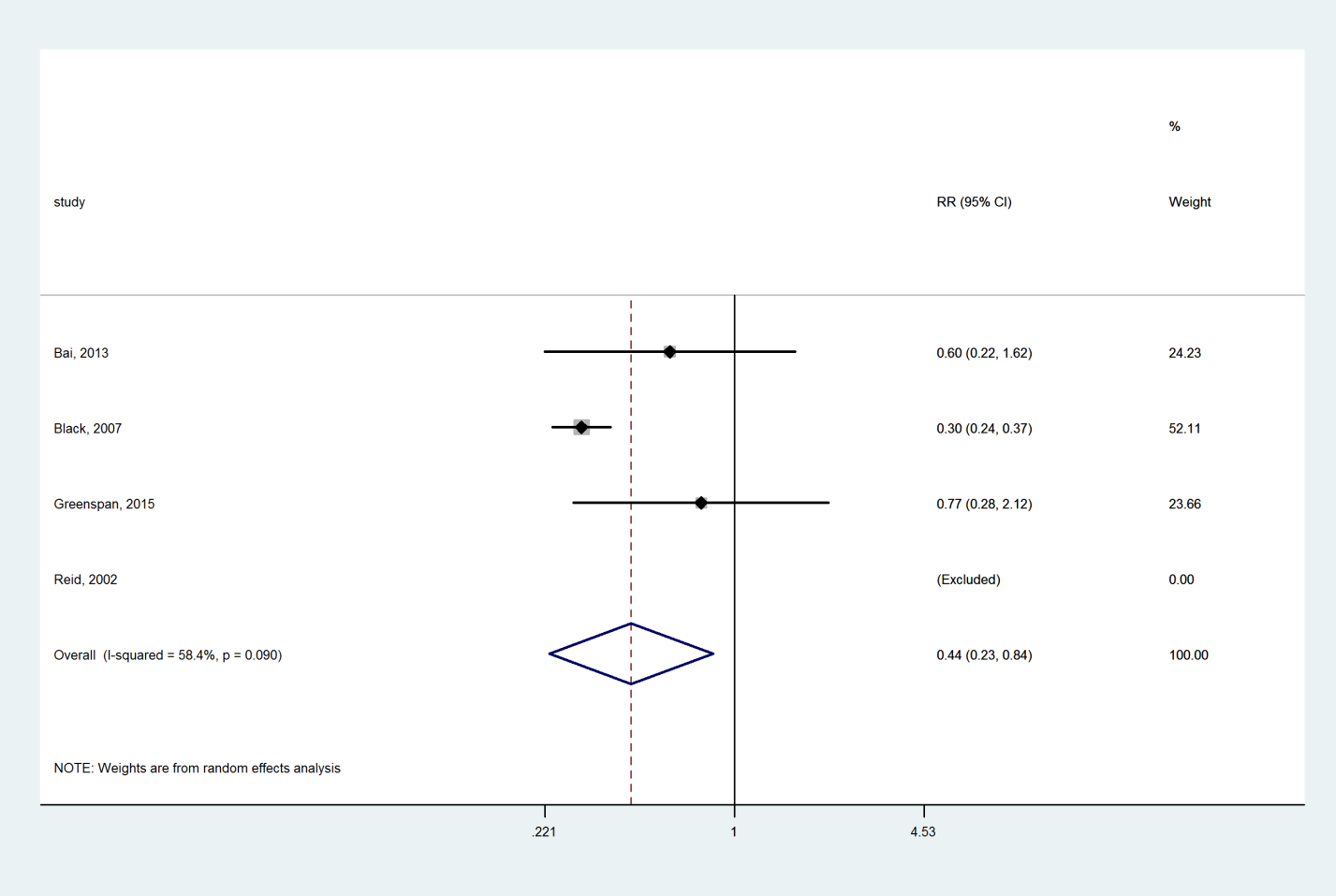
### Denosumab compared with Placebo



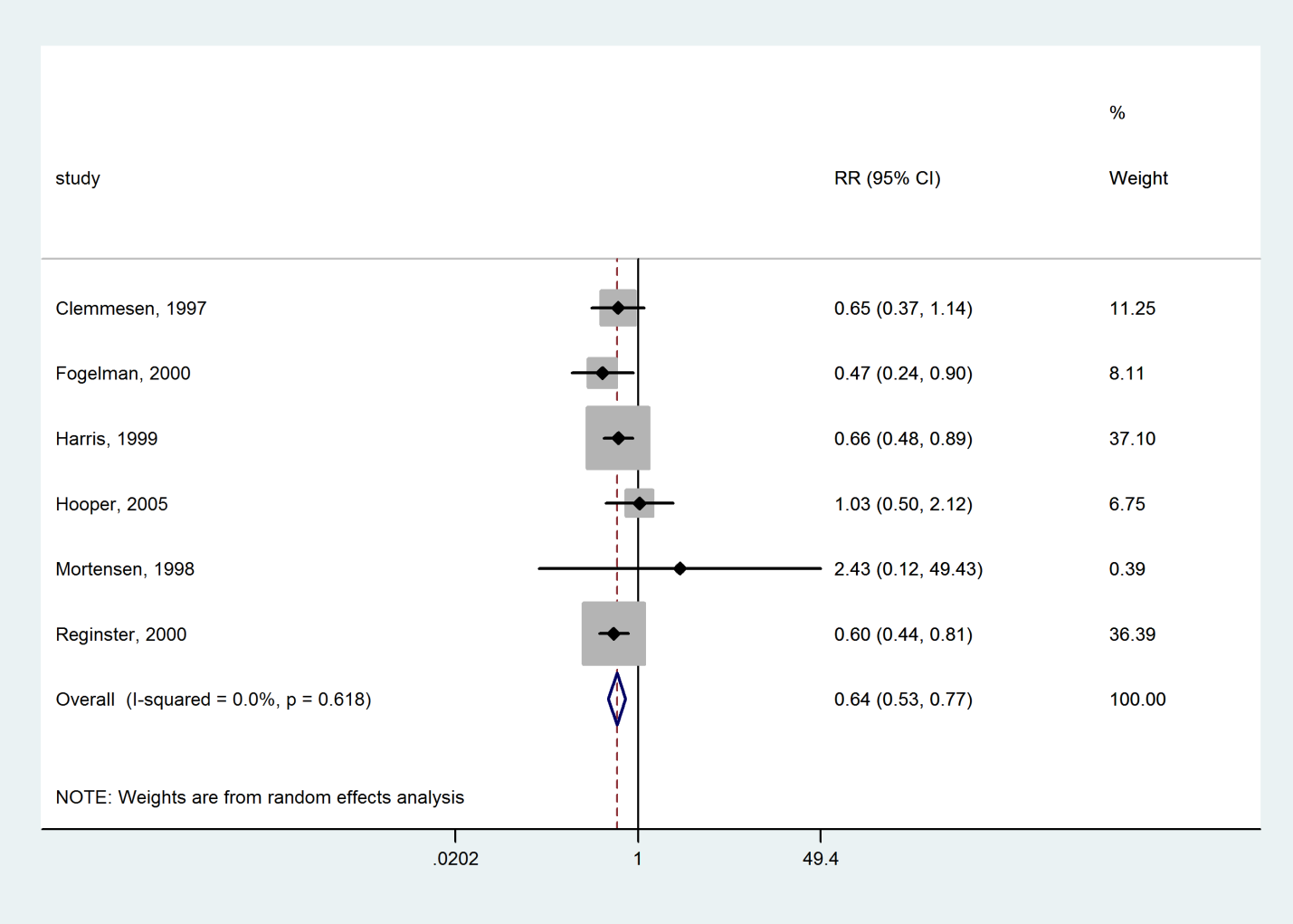
### Raloxifene compared with Placebo



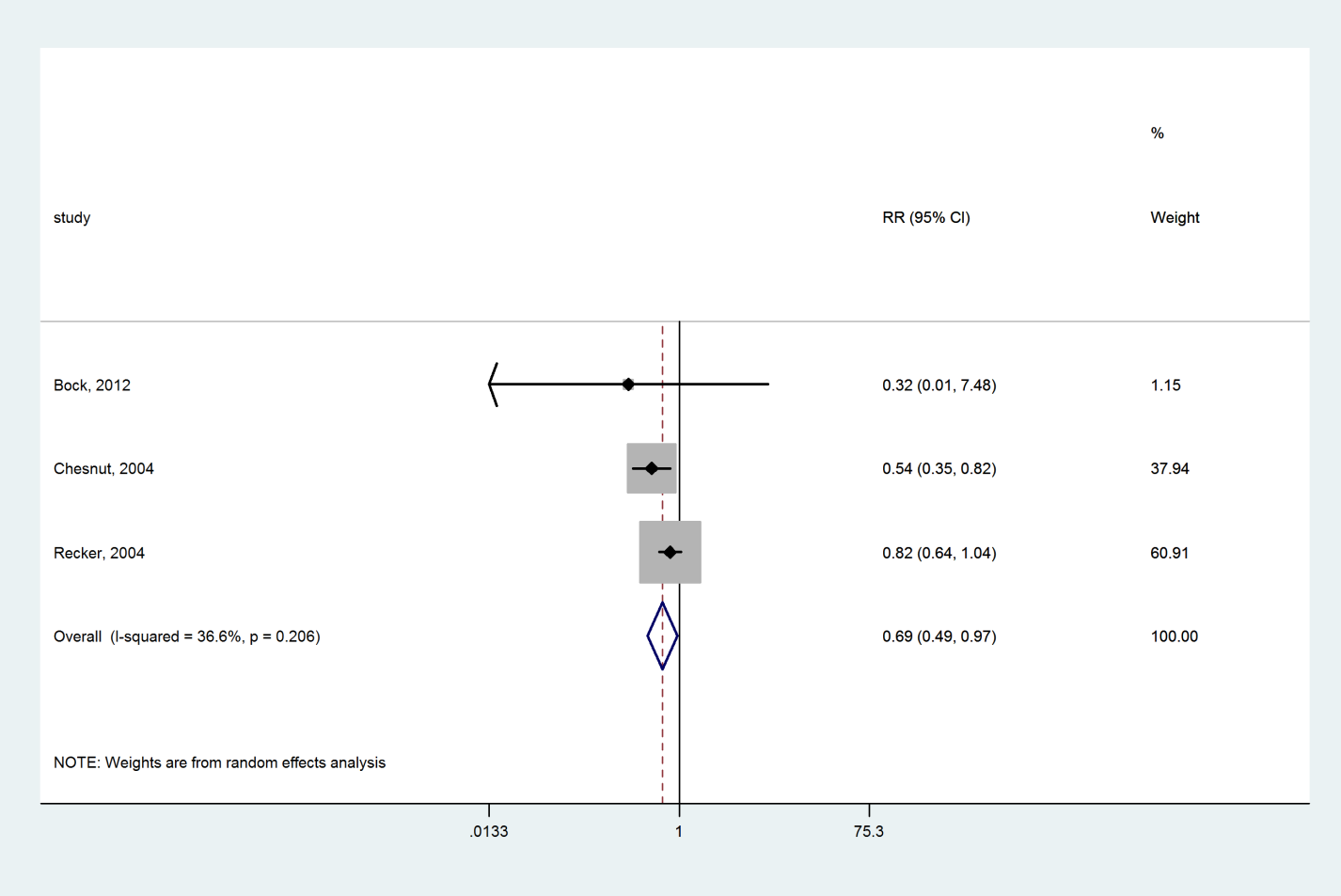
### Zoledronate compared with Placebo



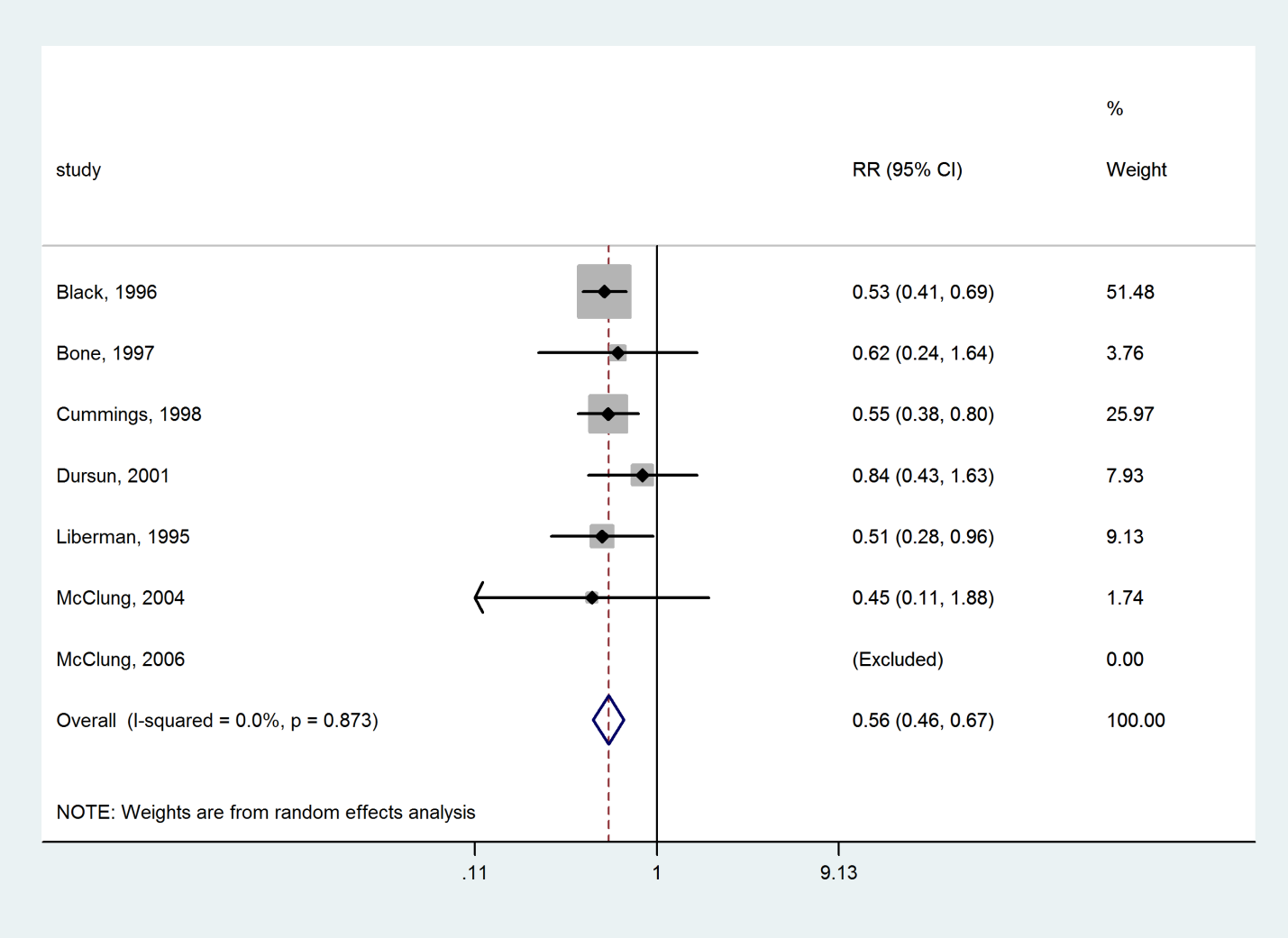
### Risedronate compared with Placebo



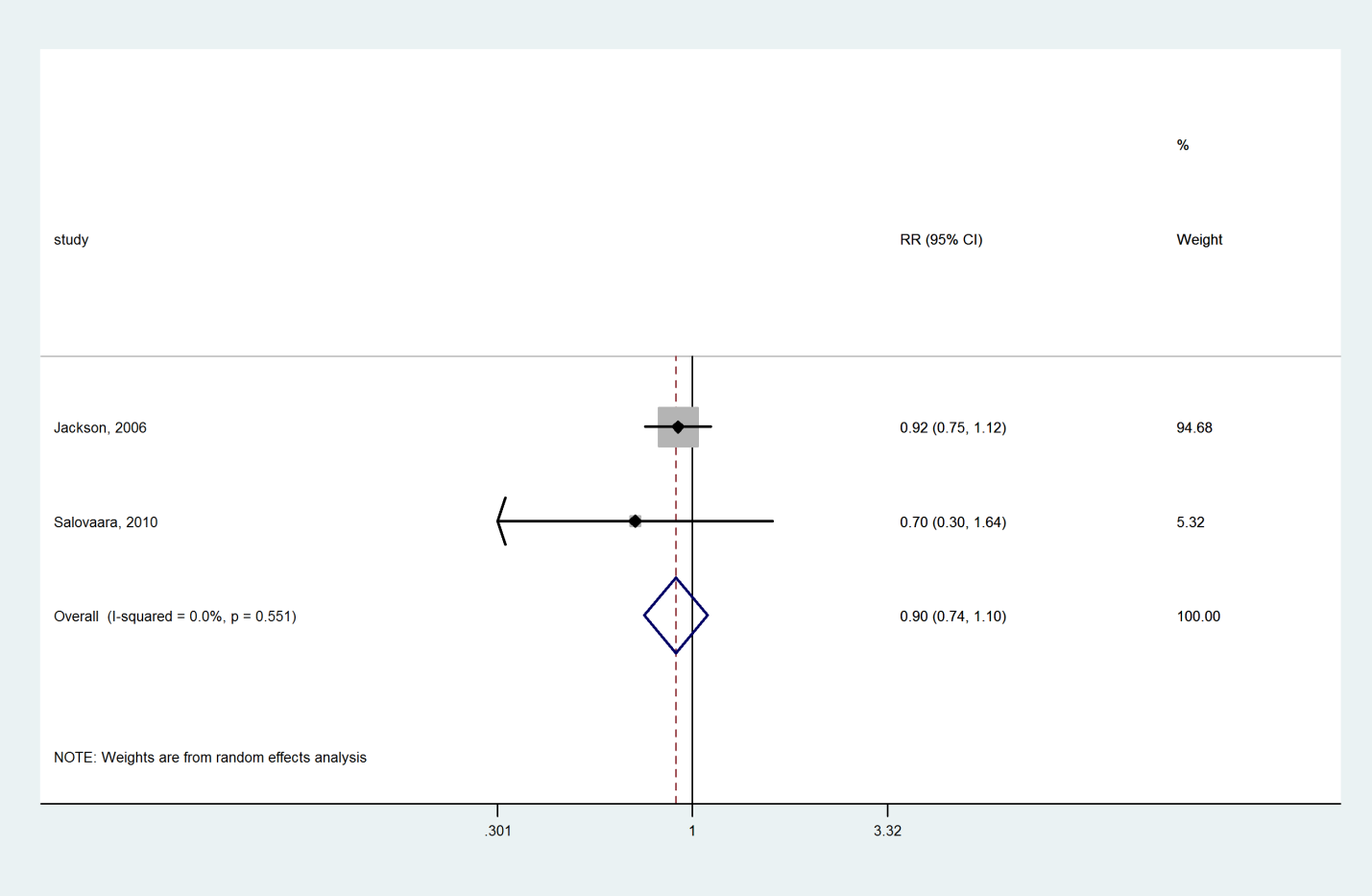
### Ibandronate compared with Placebo



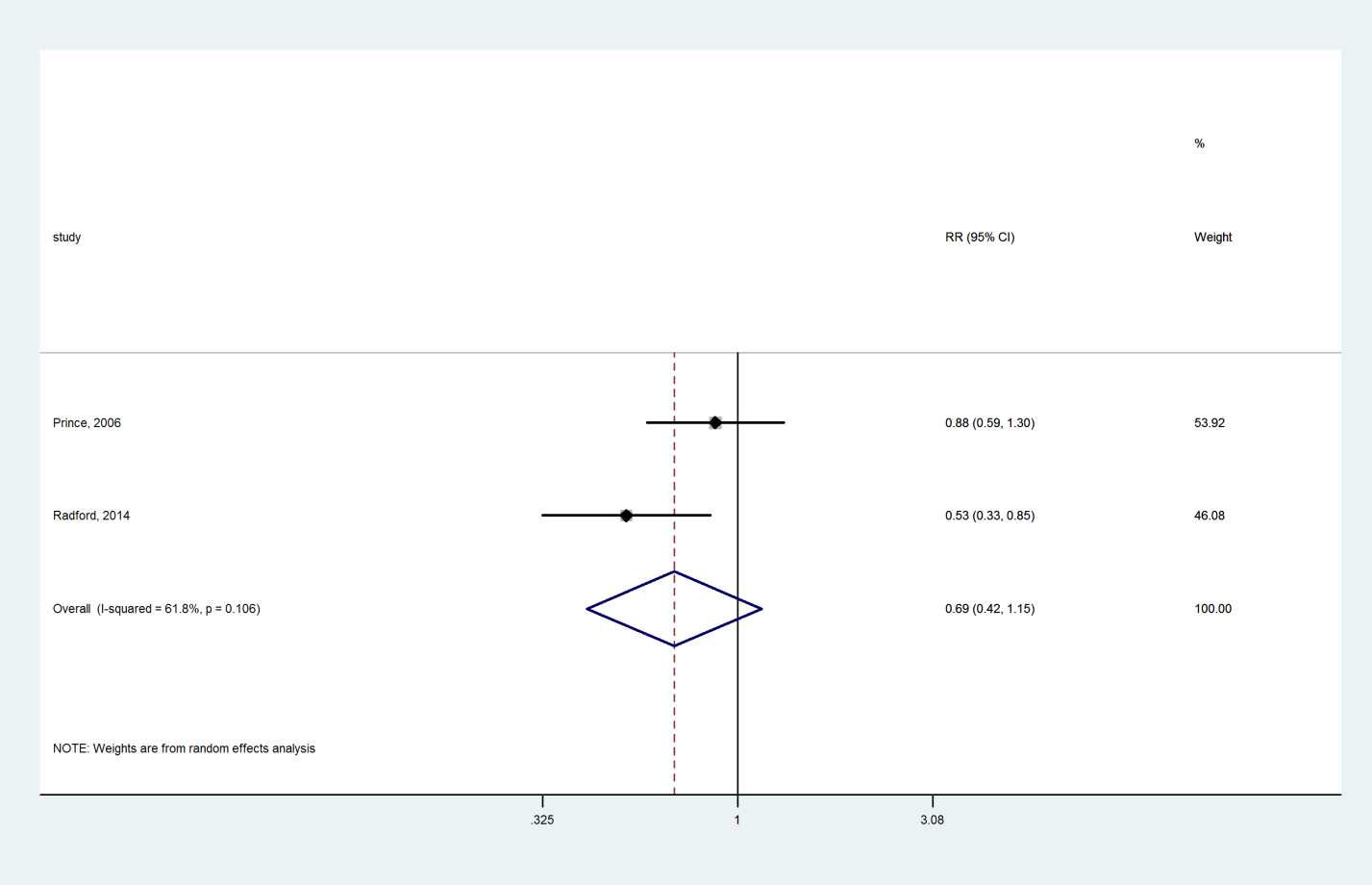
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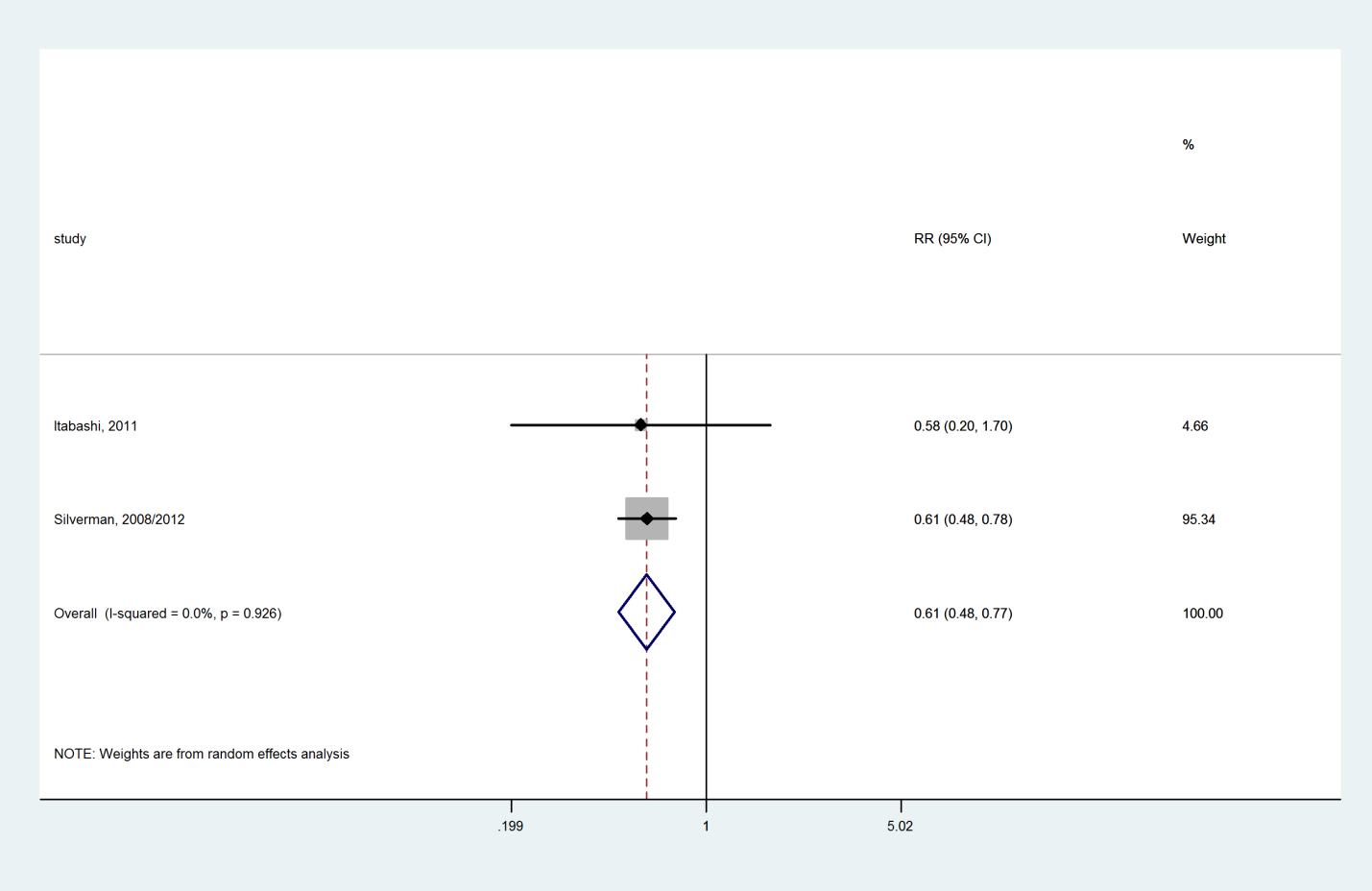
### Vitamin D+Calcium compared with Placebo



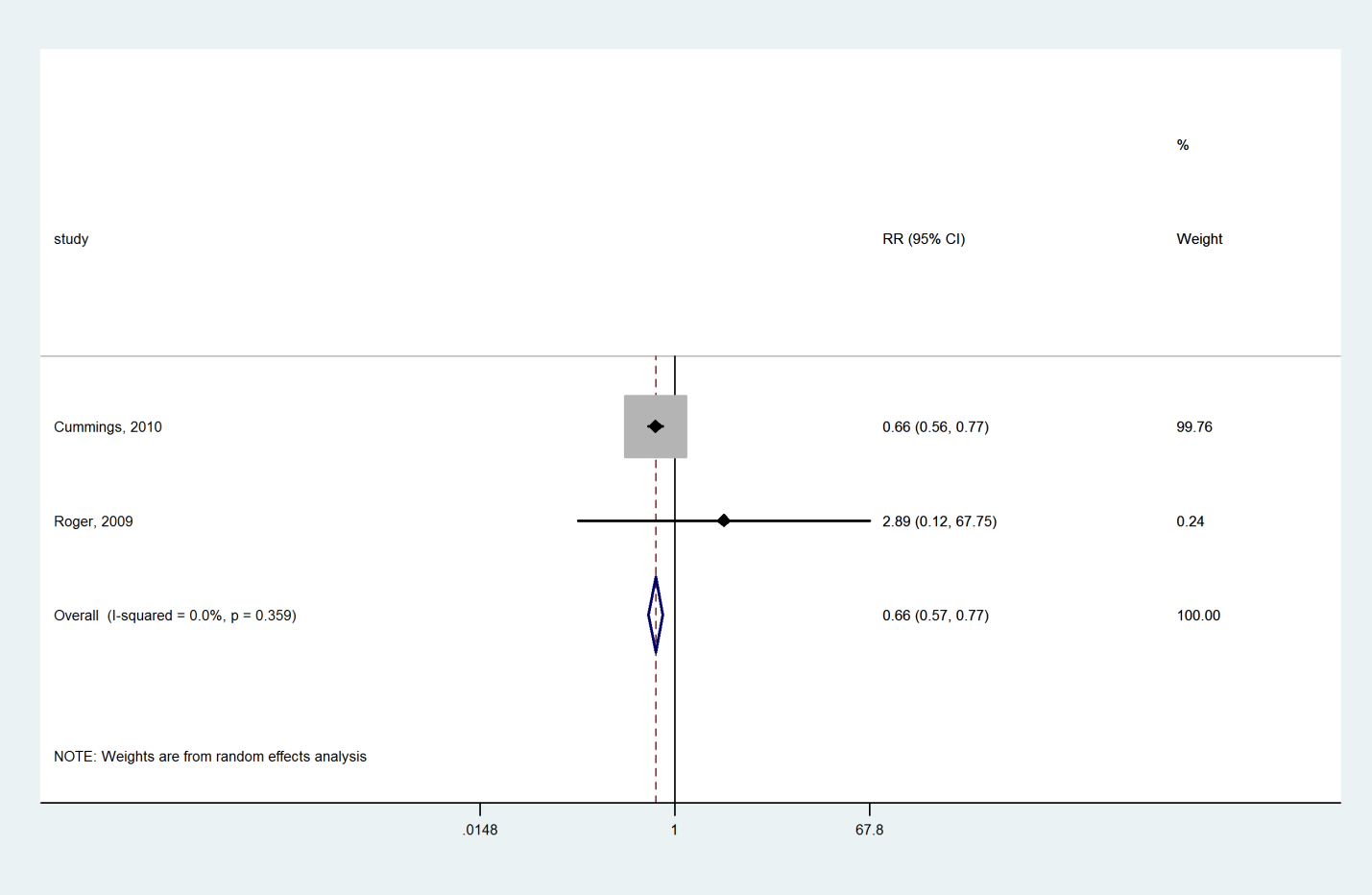
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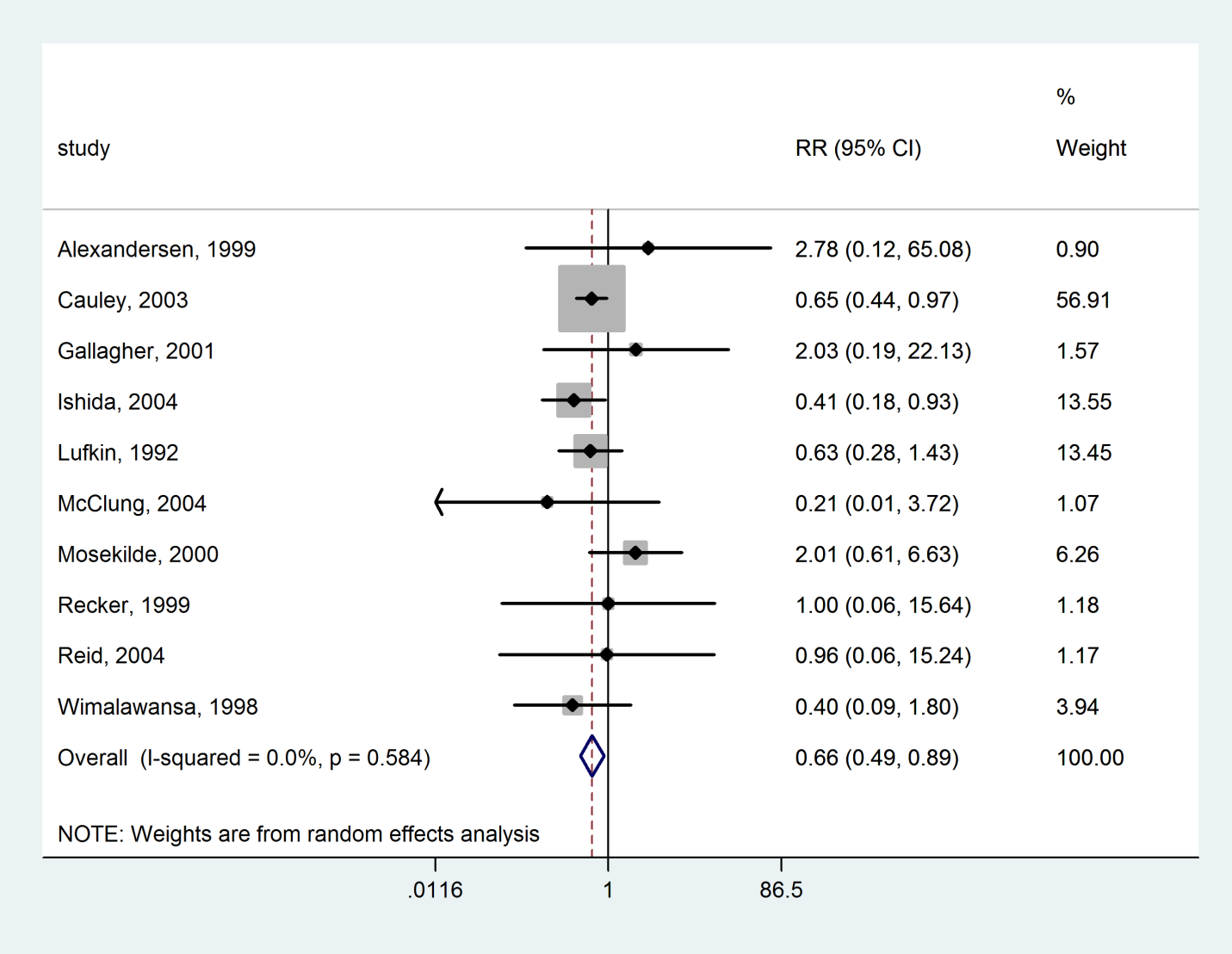
### Bazedoxifene compared with Placebo



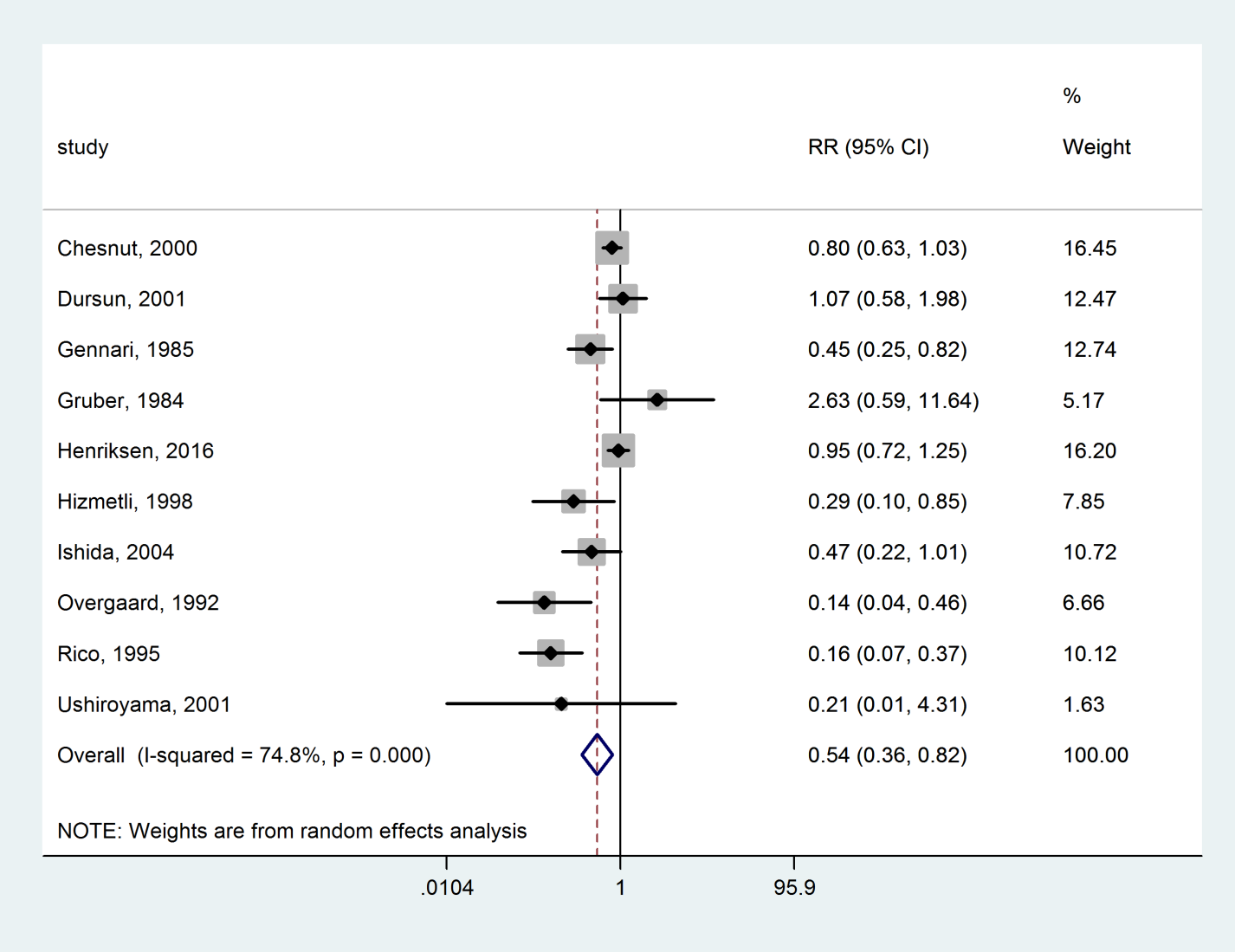
### Lasofoxifene compared with Placebo



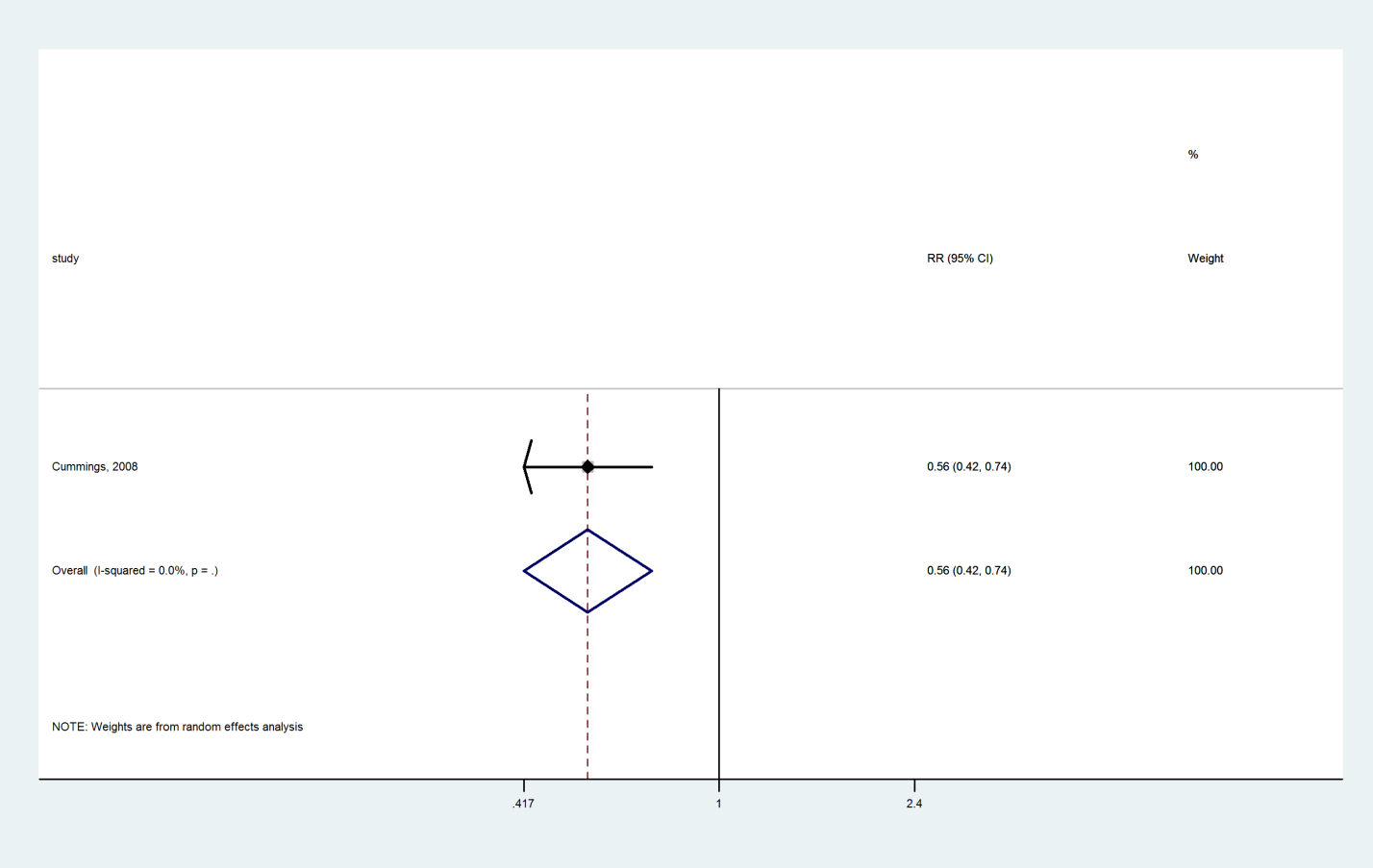
### Hormone therapy compared with Placebo



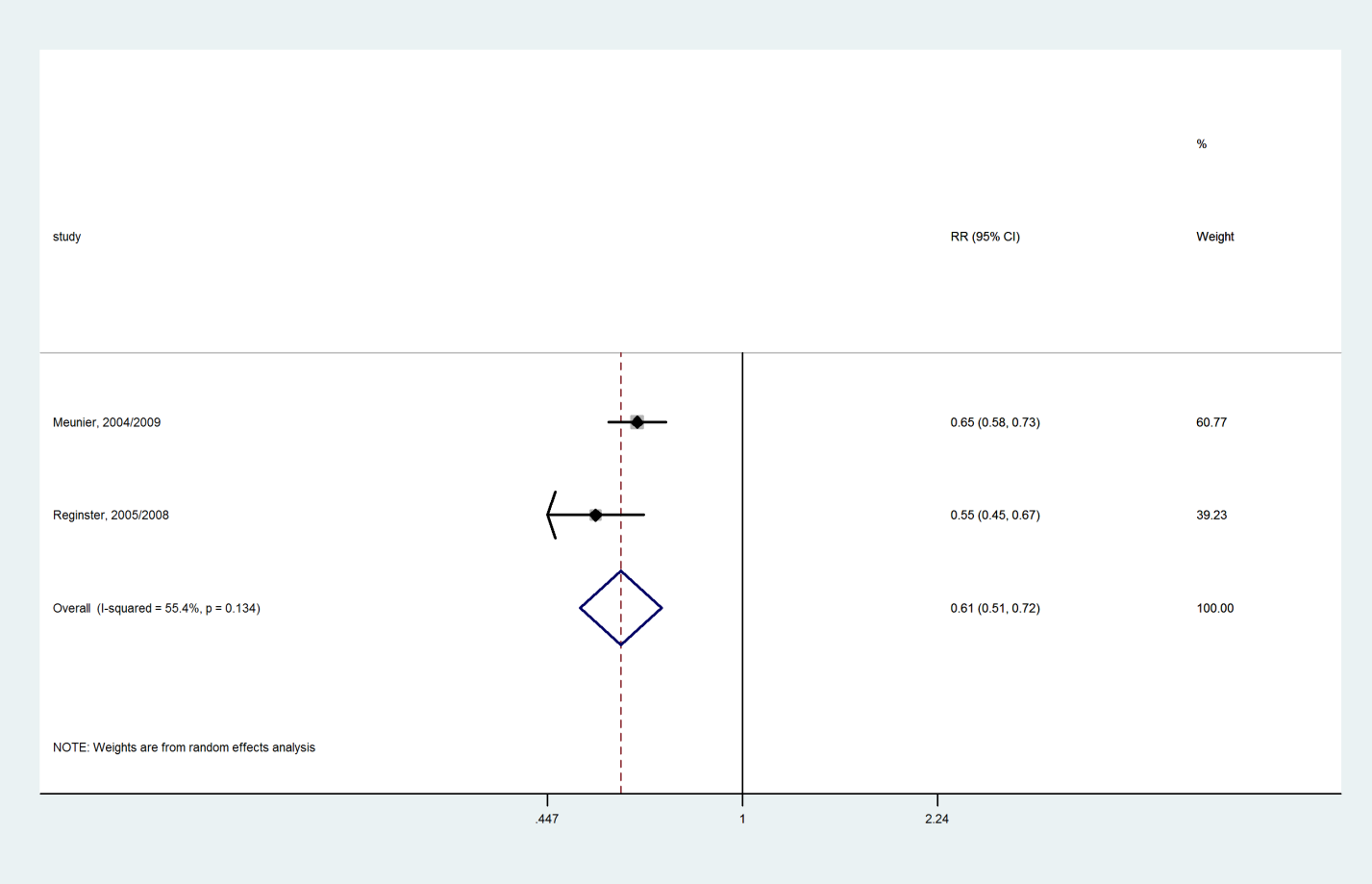
### Calcitonin compared with Placebo



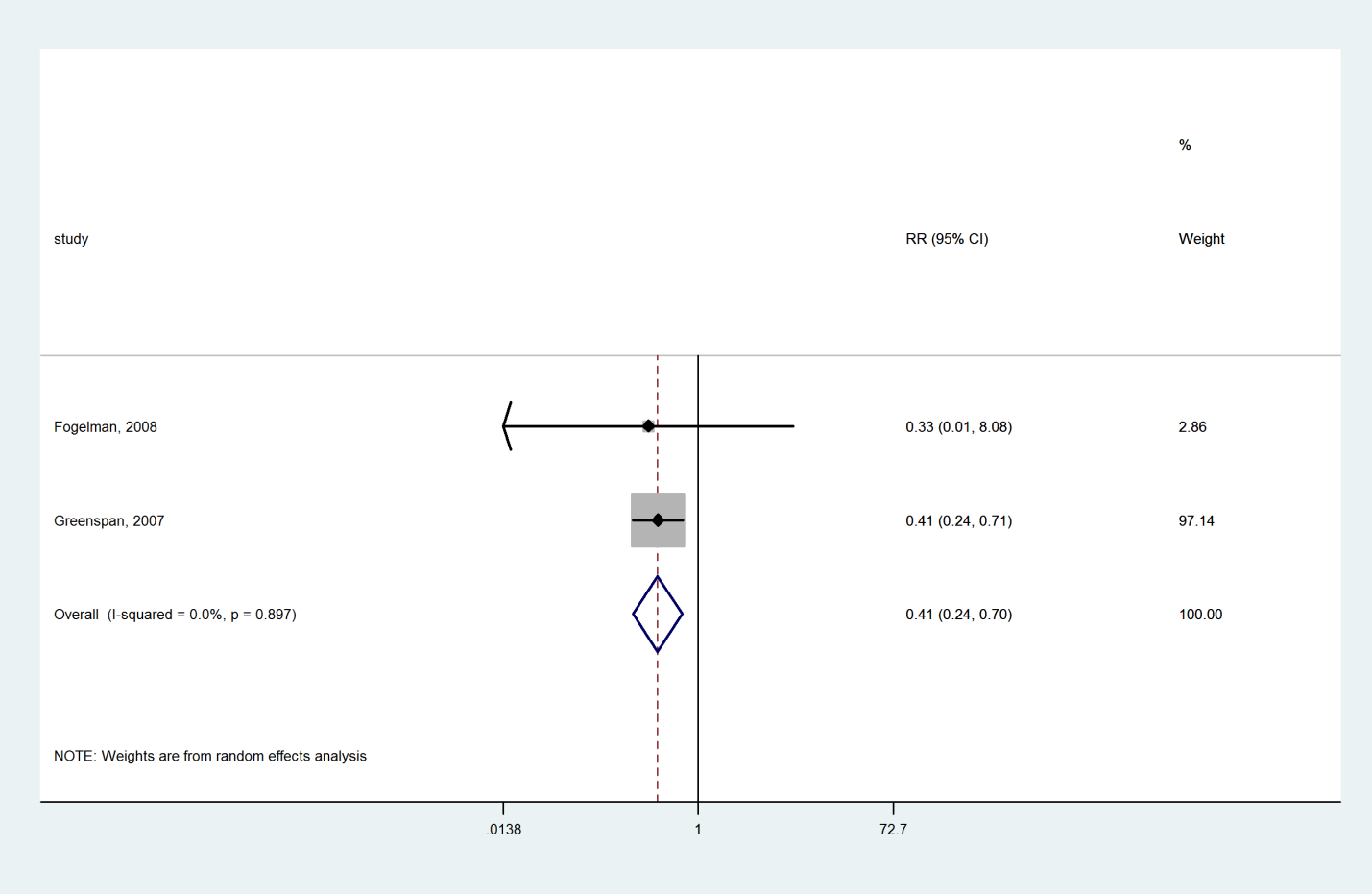
### Tibolone compared with Placebo



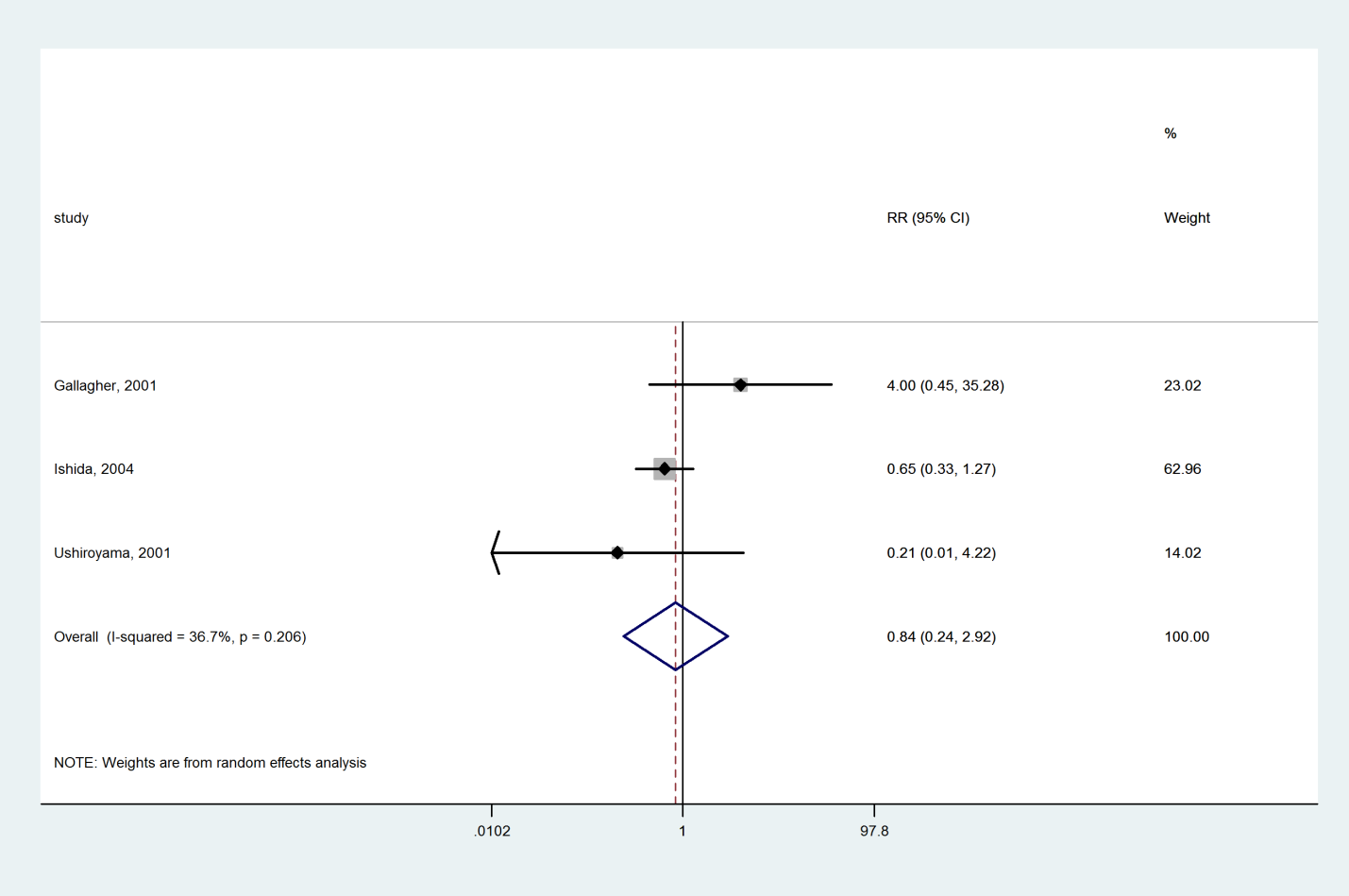
### Strontium ranelate compared with Placebo



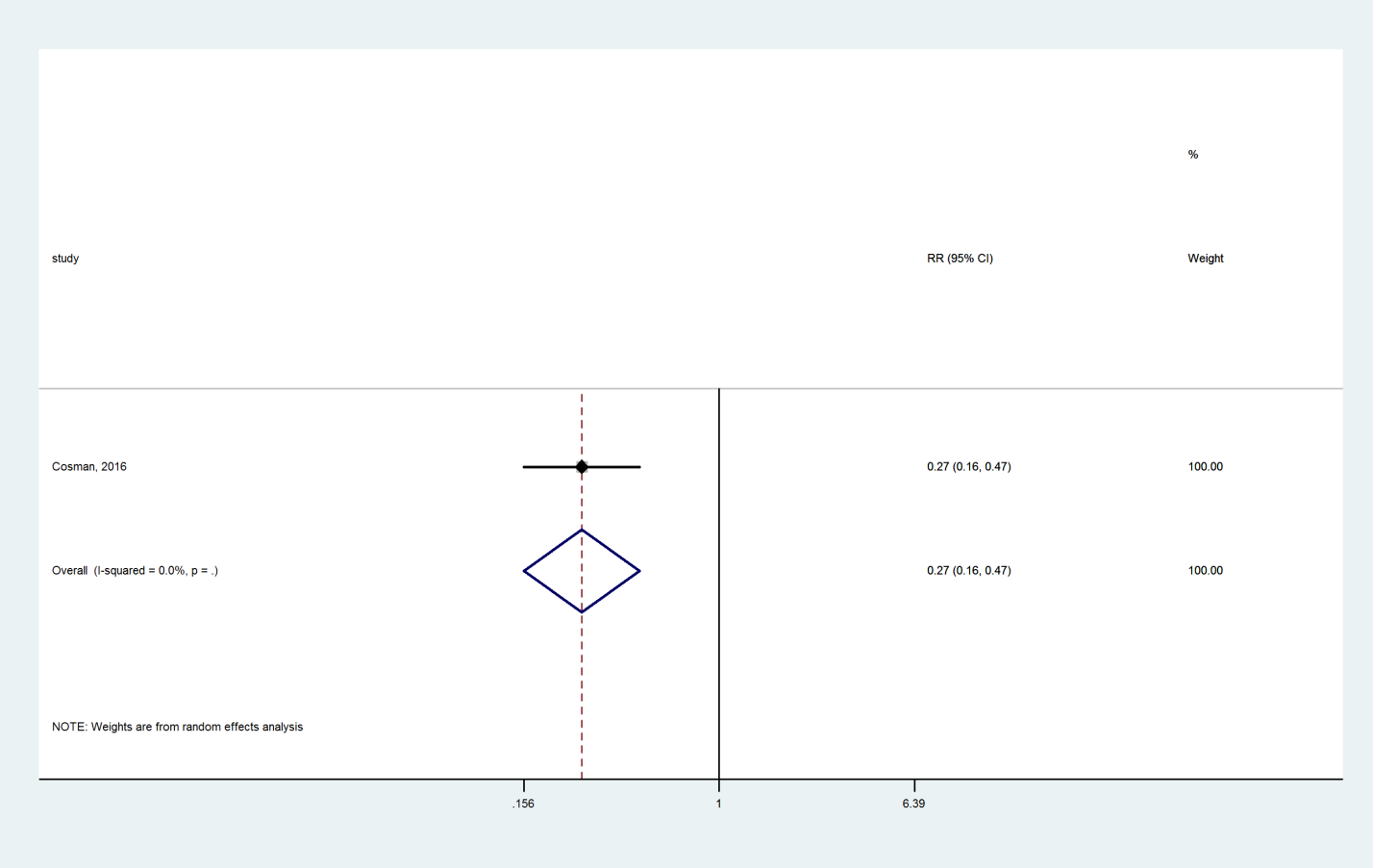
### PTH 1-84 compared with Placebo



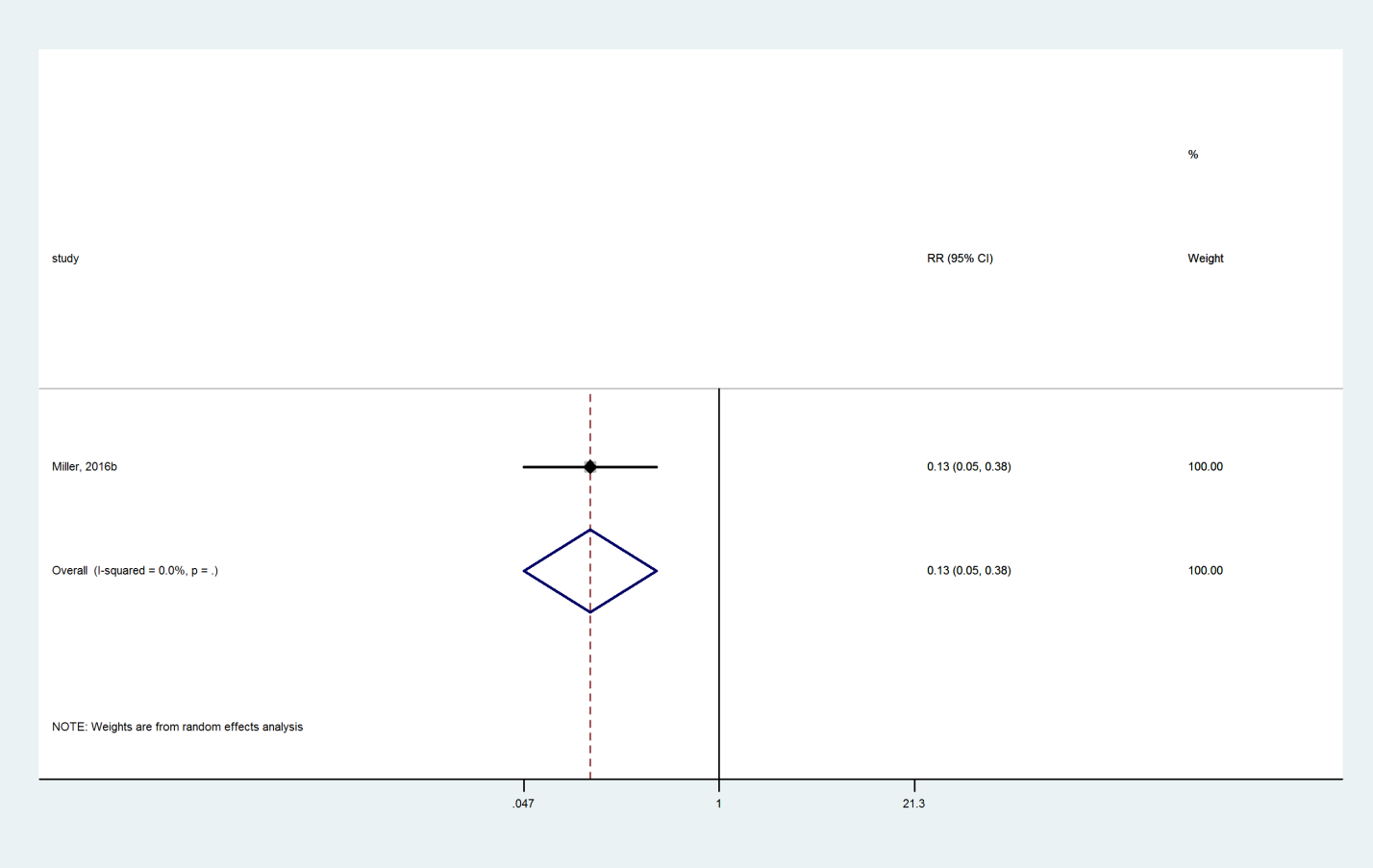
### Vitamin D compared with Placebo



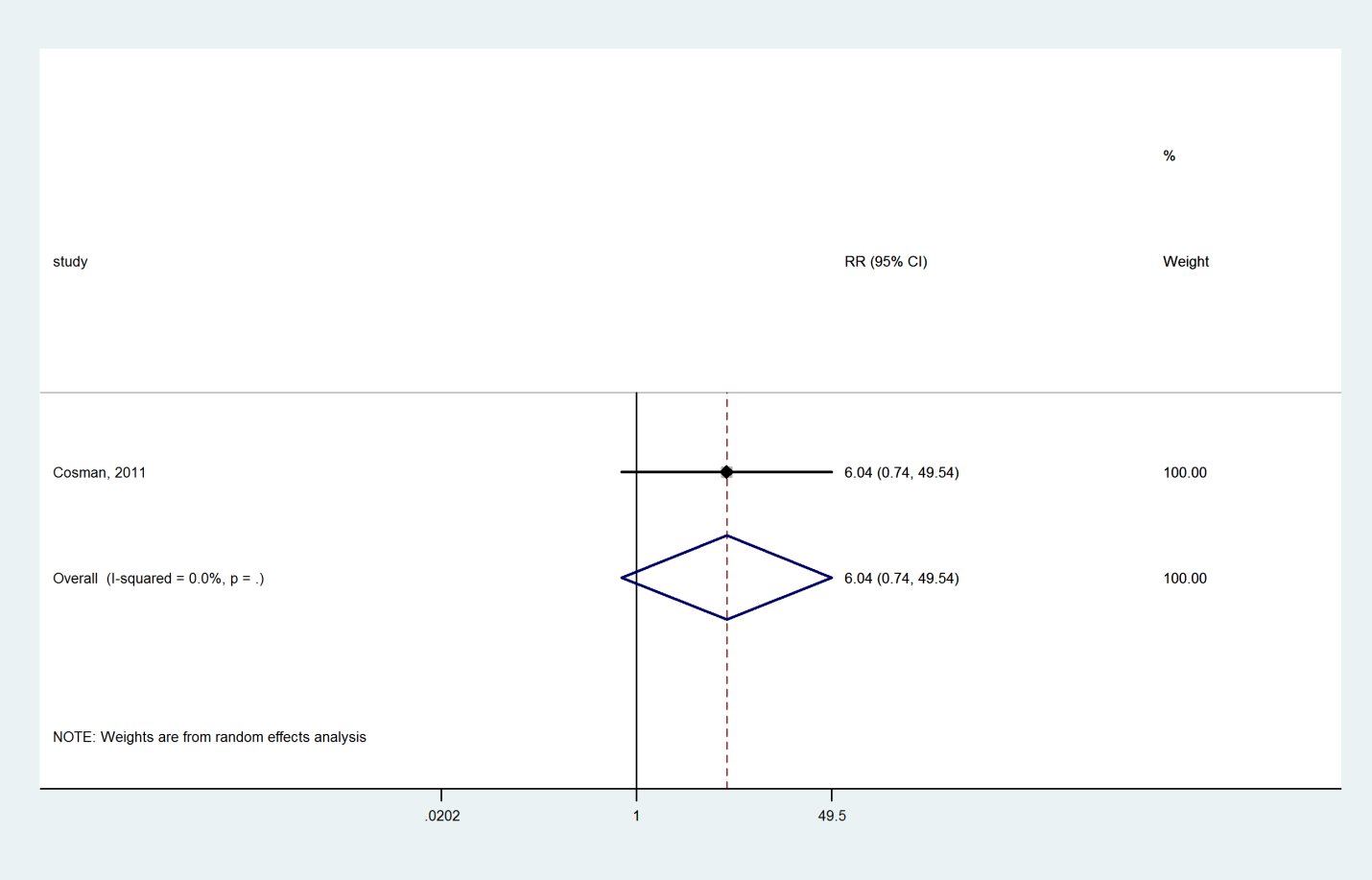
### Romosozumab compared with Placebo



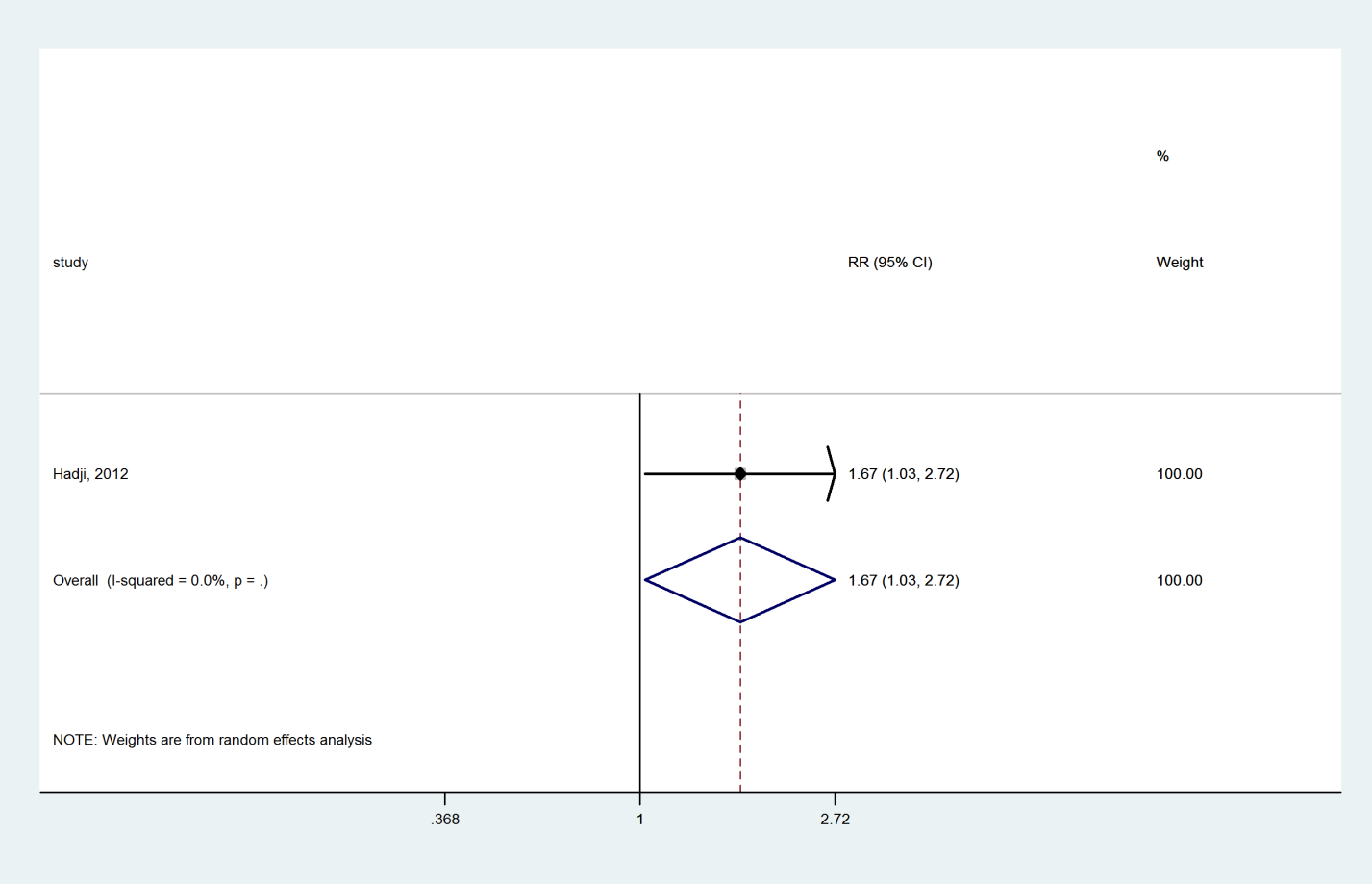
### Abaloparatide compared with Placebo



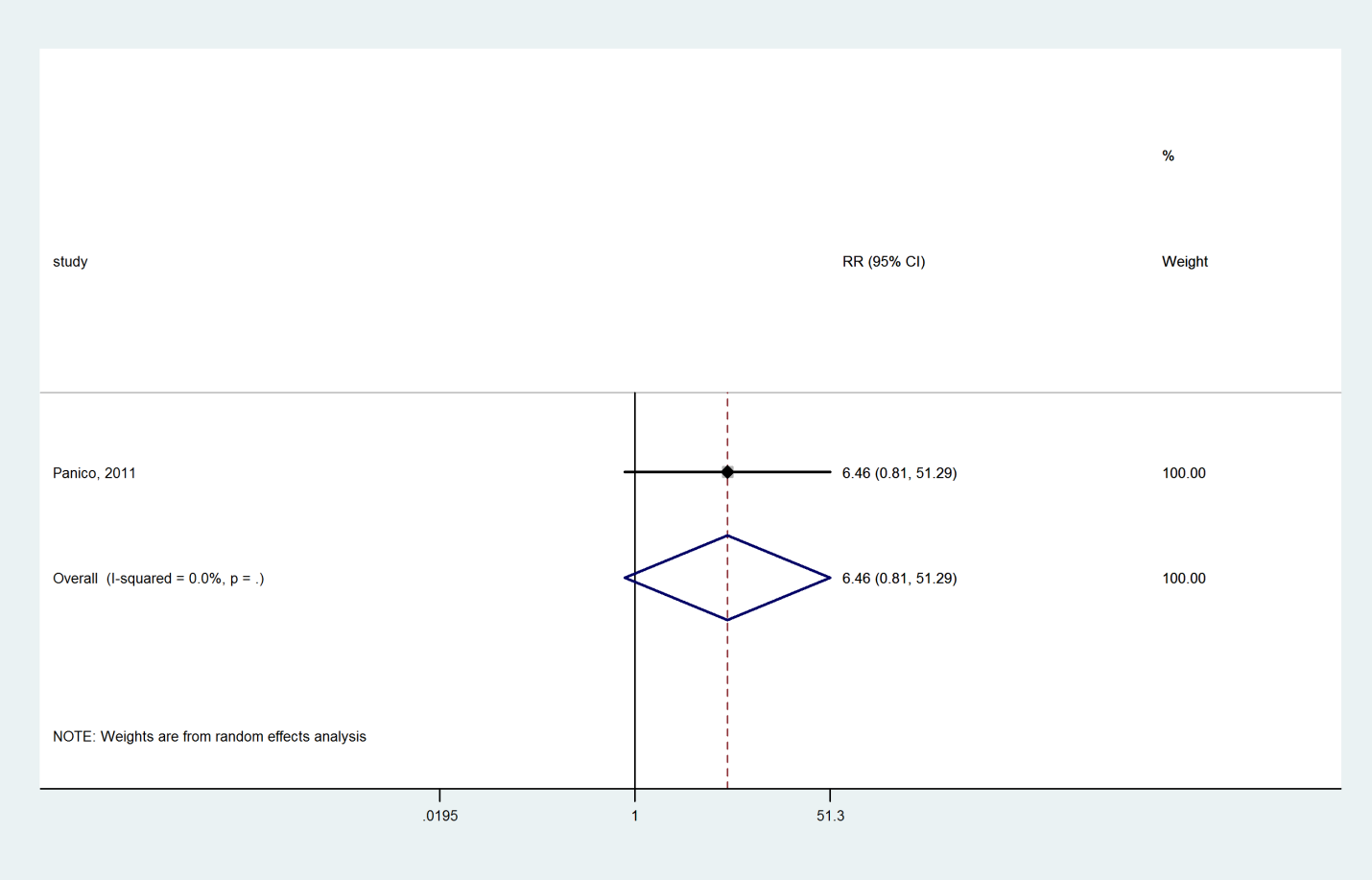
### Zoledronate compared with Teriparatide



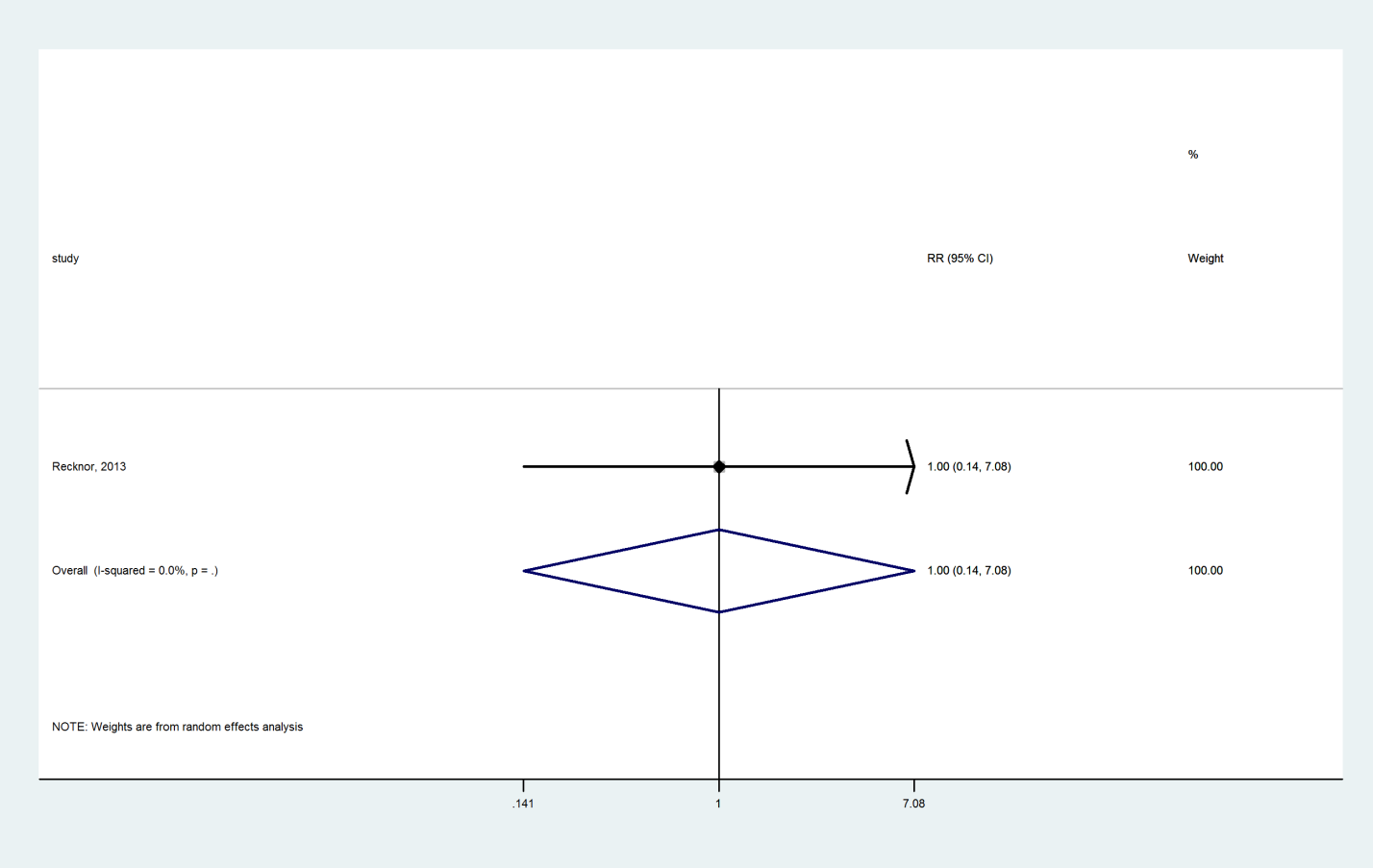
### Risedronate compared with Teriparatide



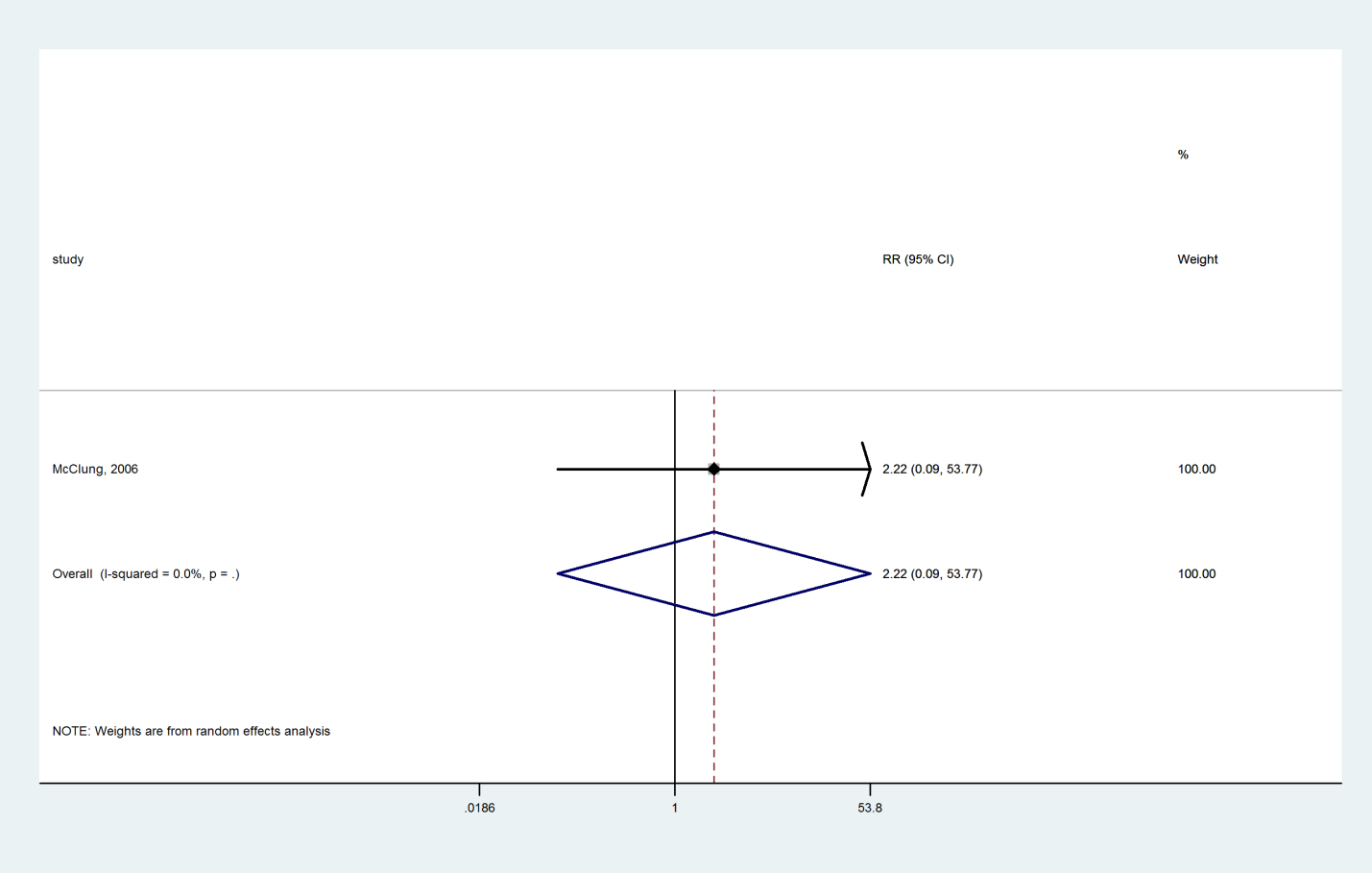
### Alendronate compared with Teriparatide



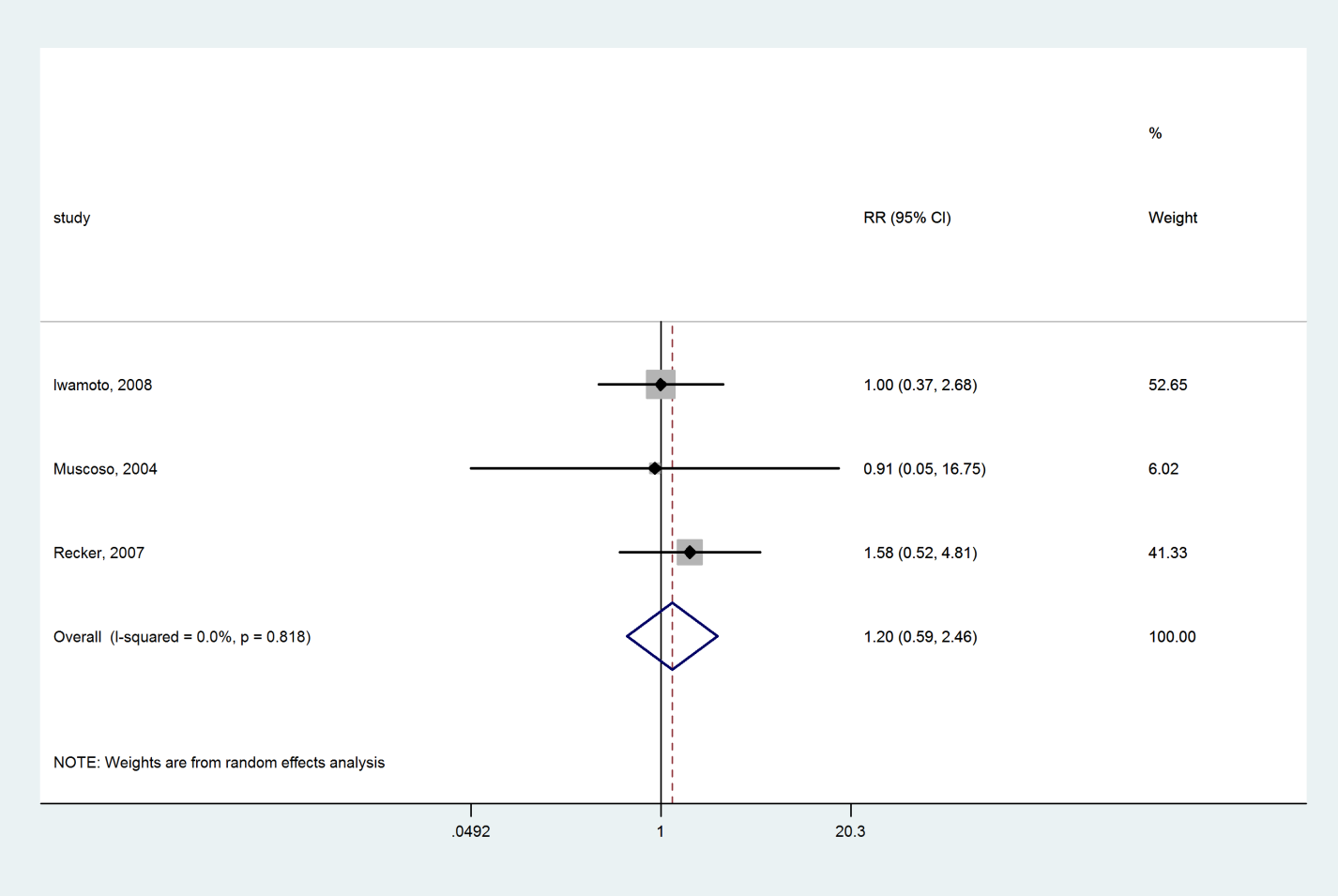
### Ibandronate compared with Denosumab



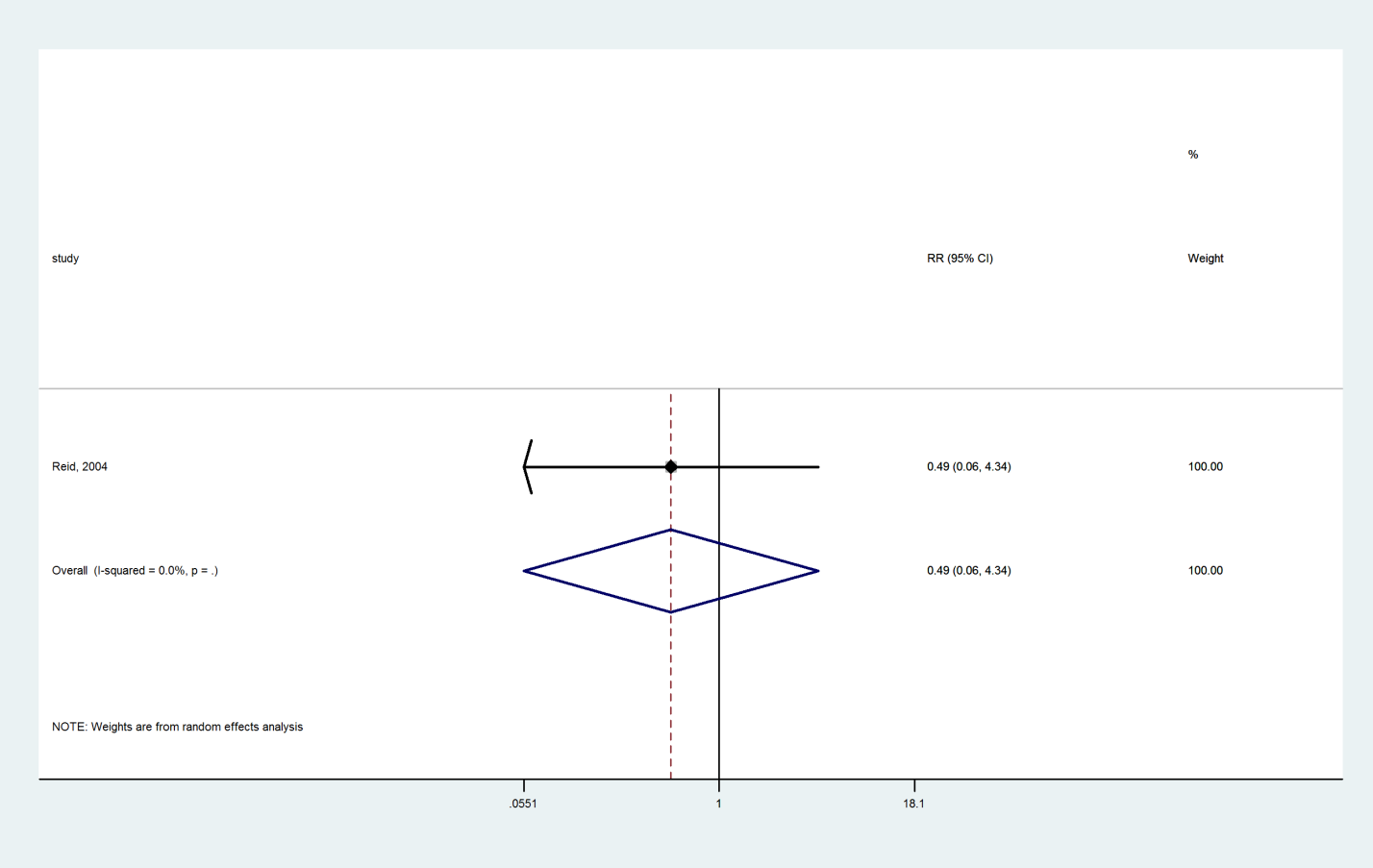
### Alendronate compared with Denosumab



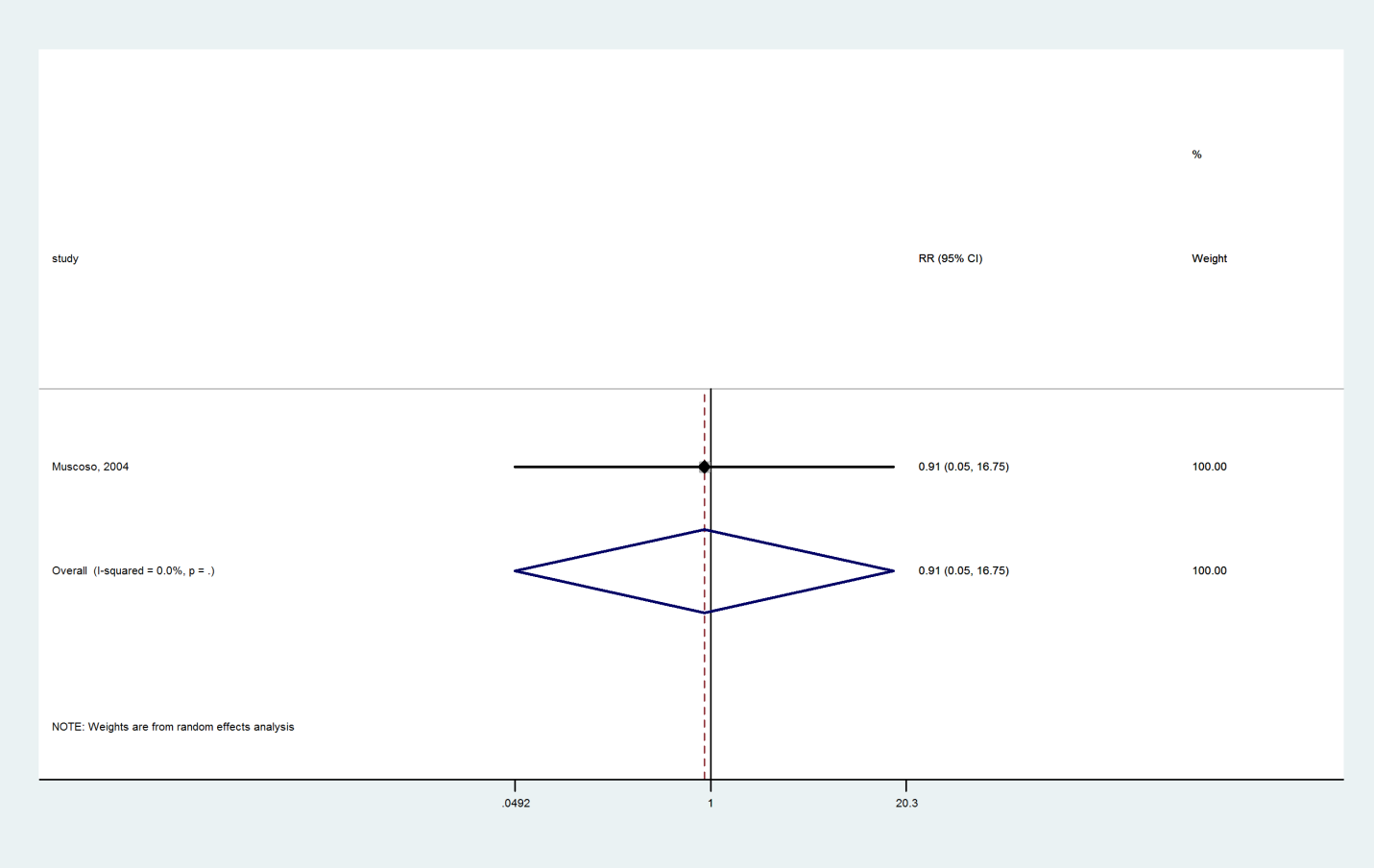
### Alendronate compared with Raloxifene



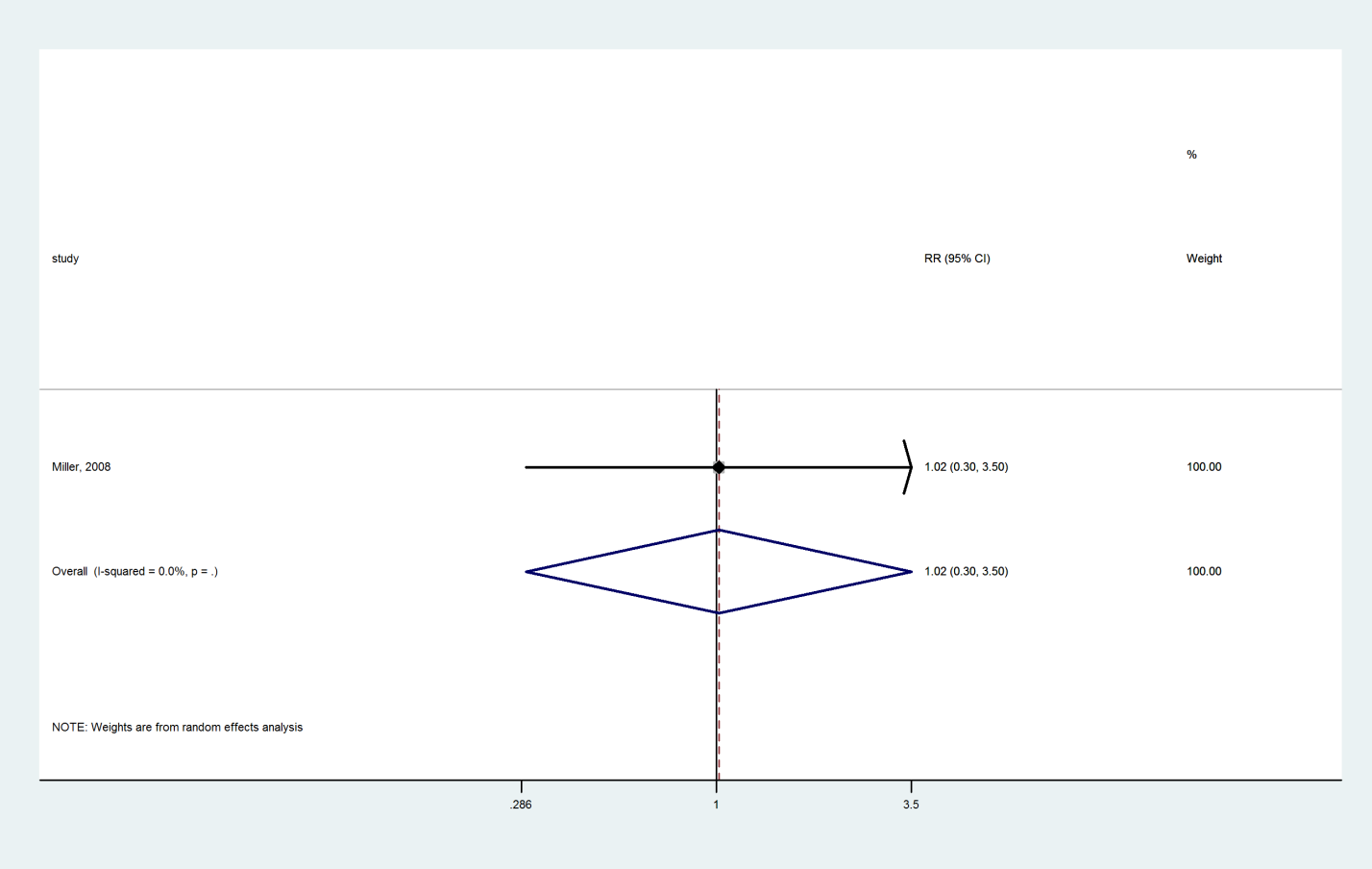
### Hormone therapy compared with Raloxifene



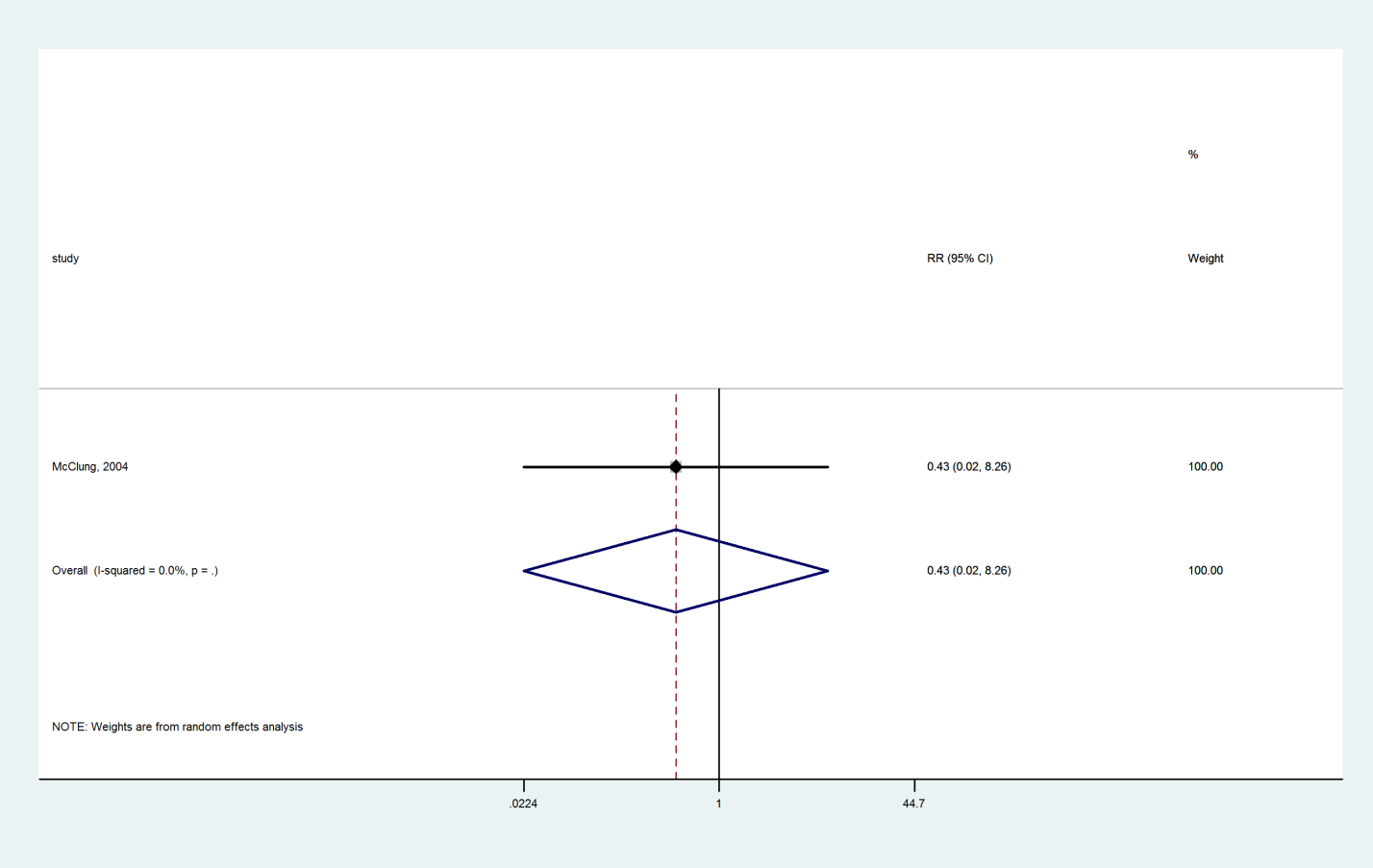
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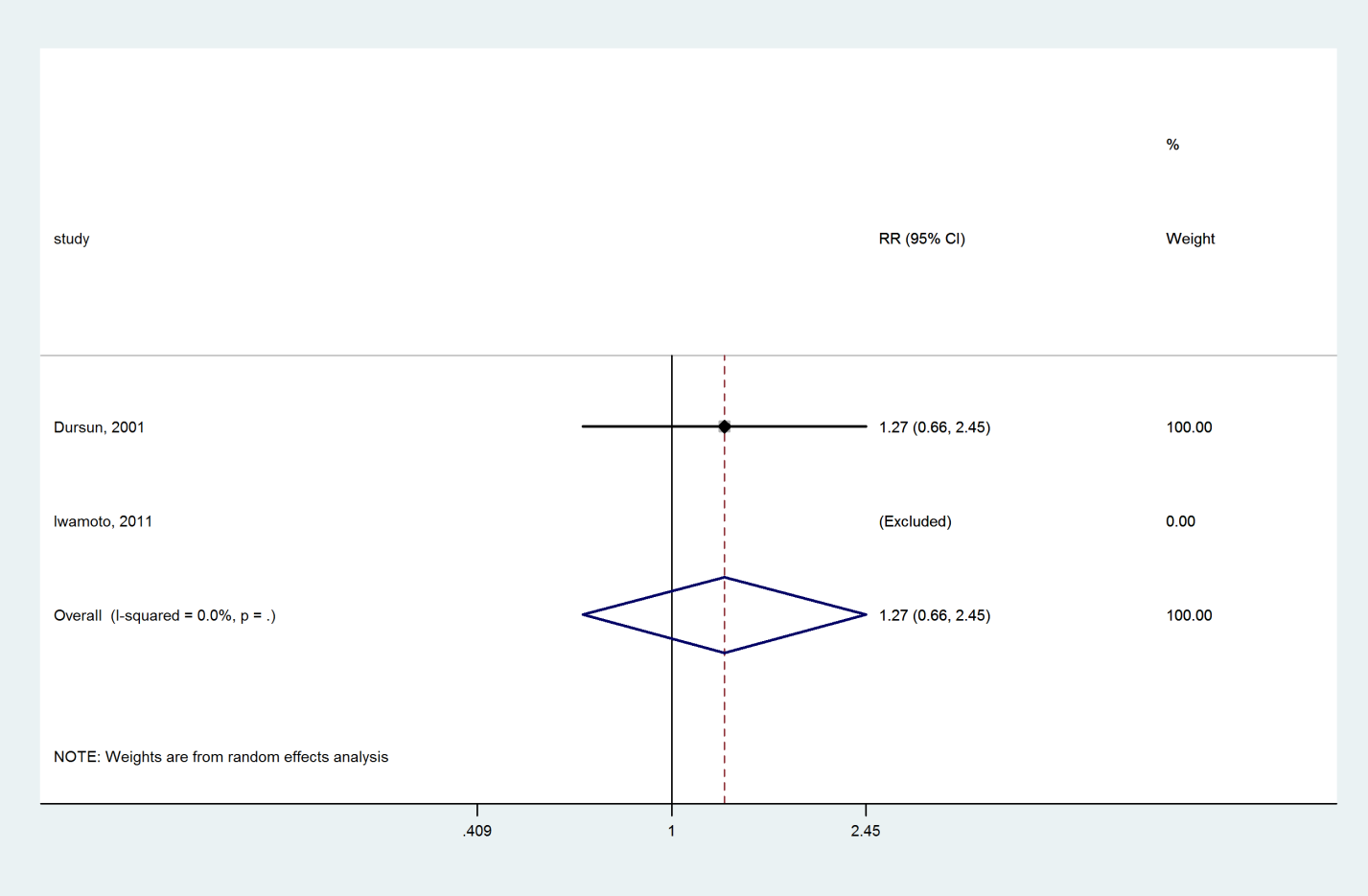
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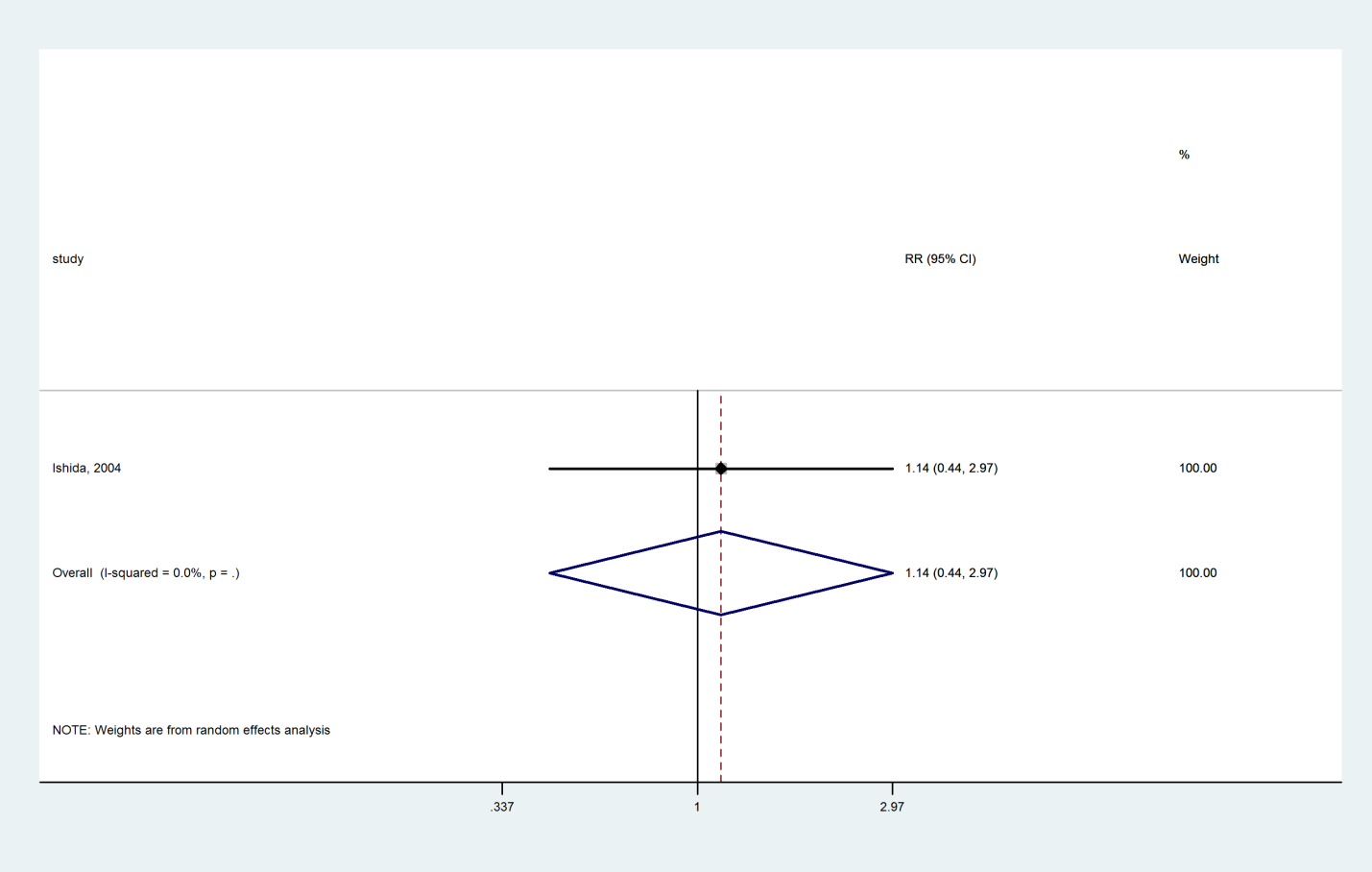
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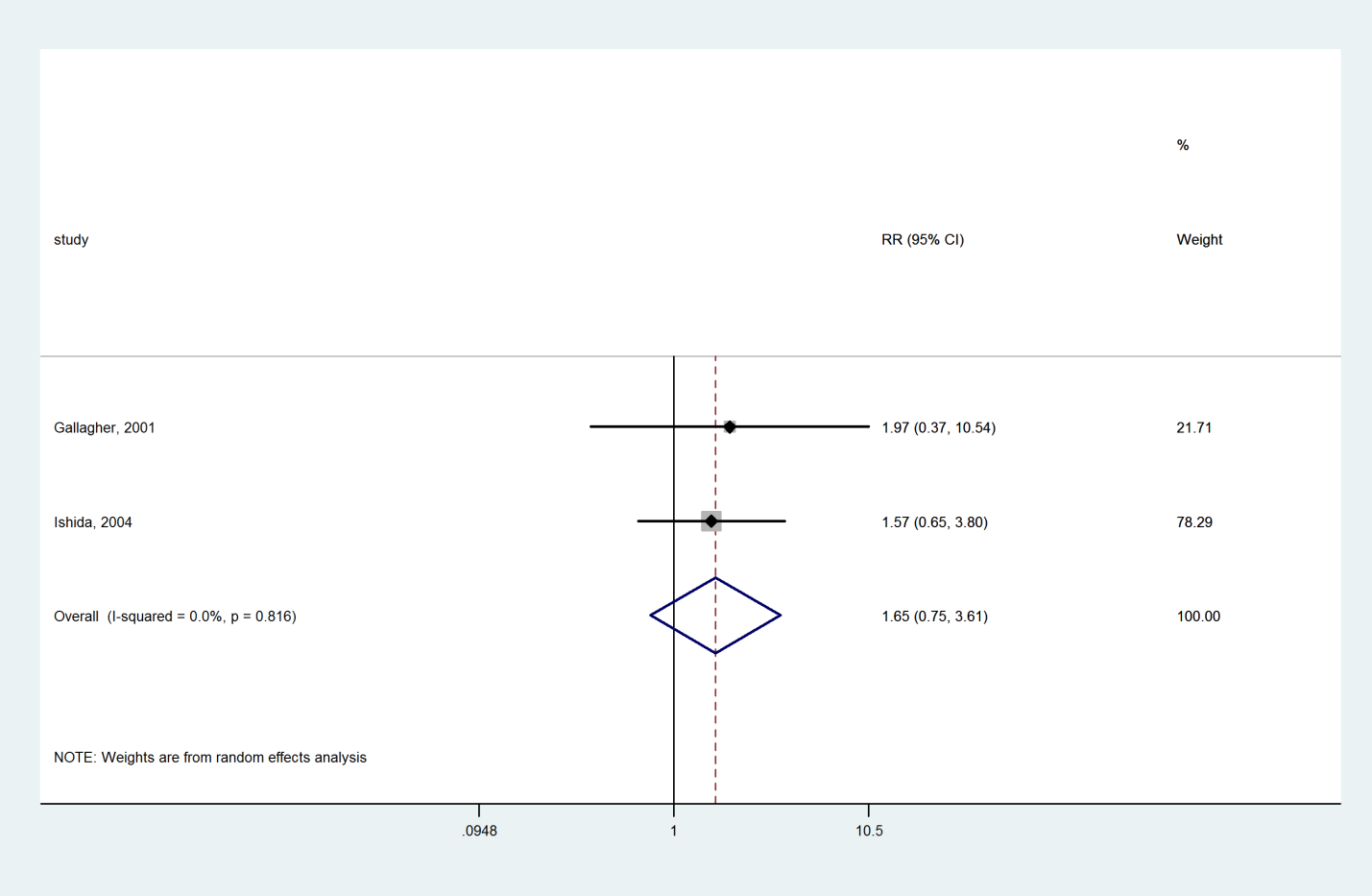
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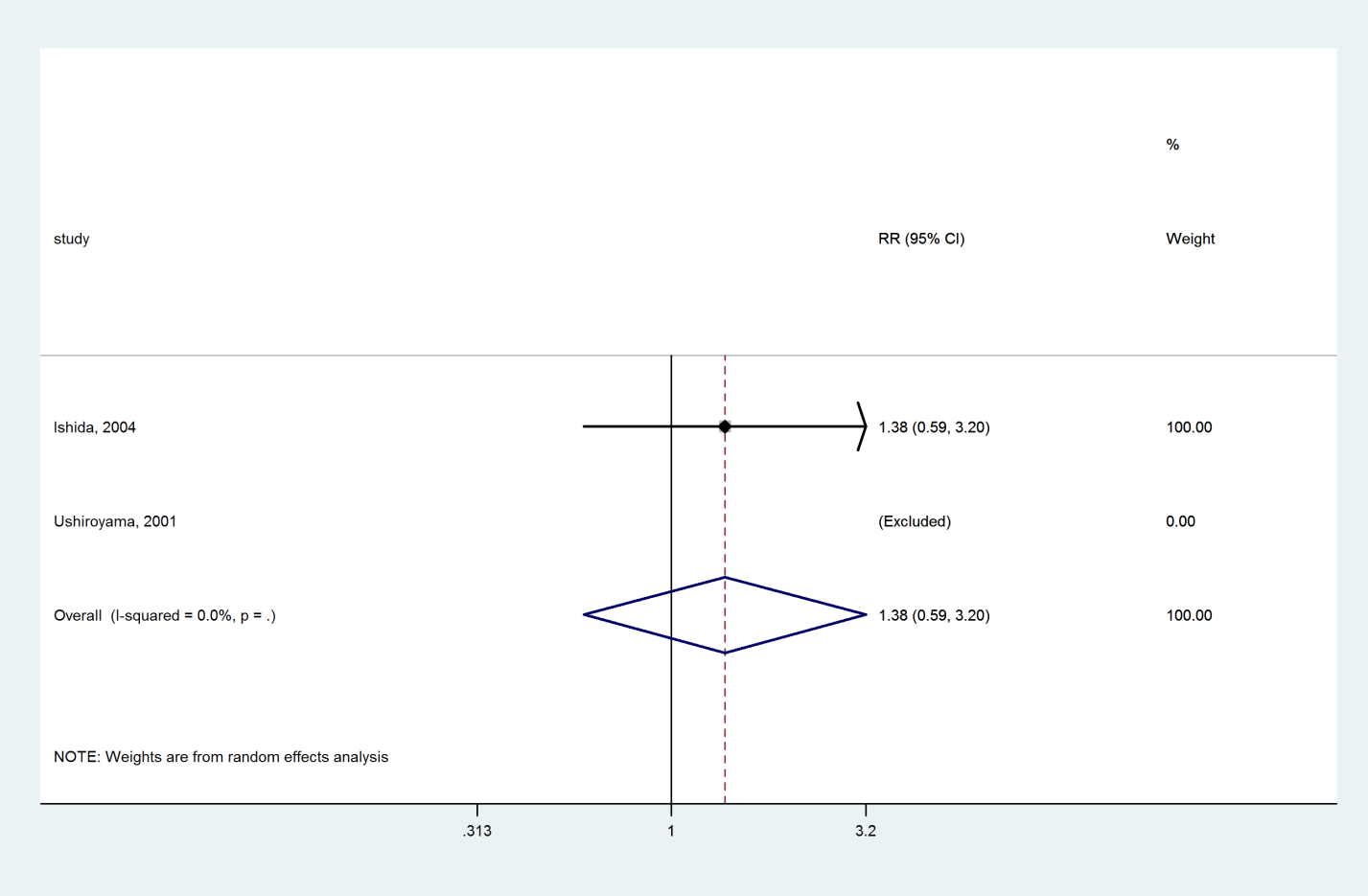
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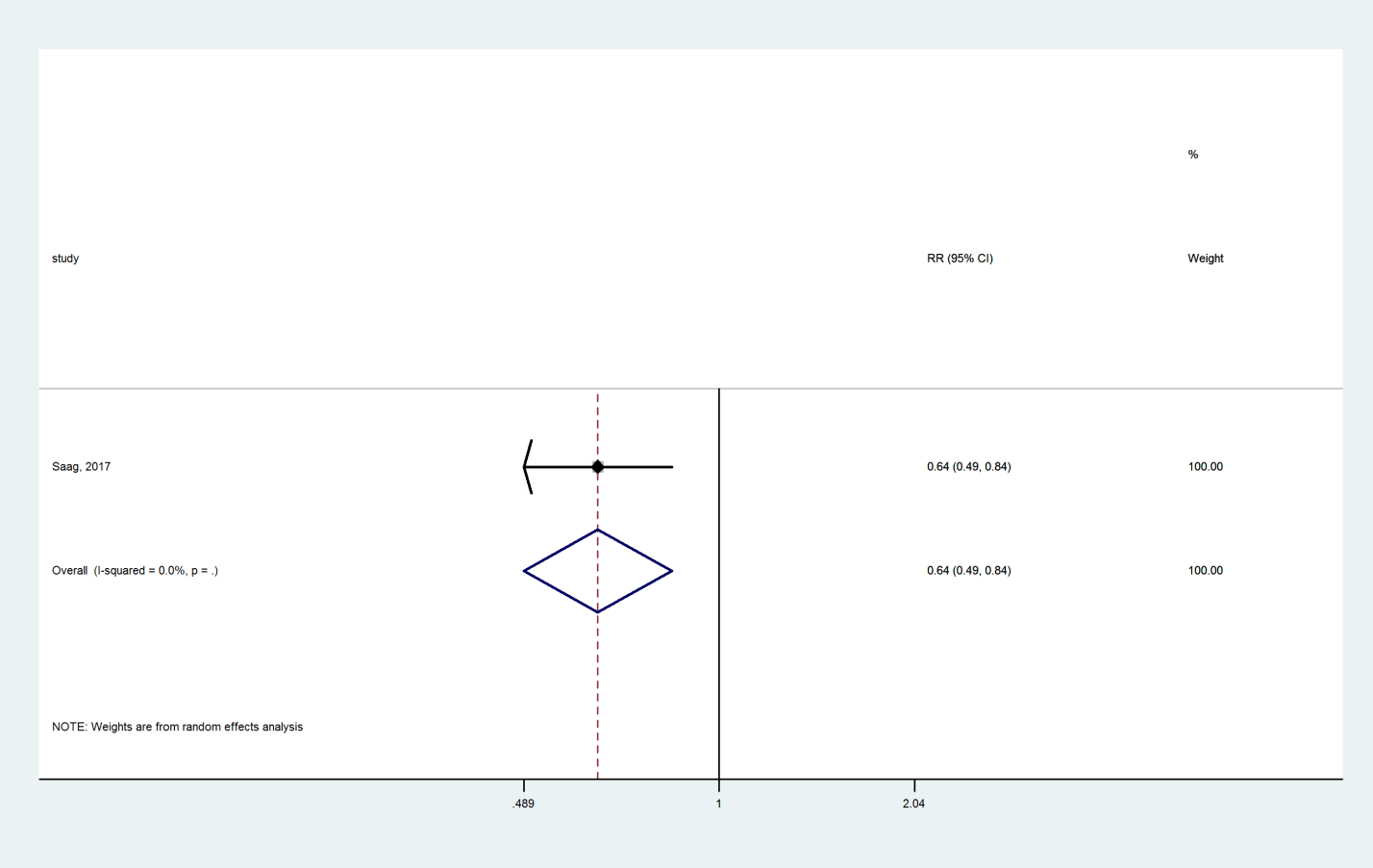
### Vitamin D compared with Hormone therapy



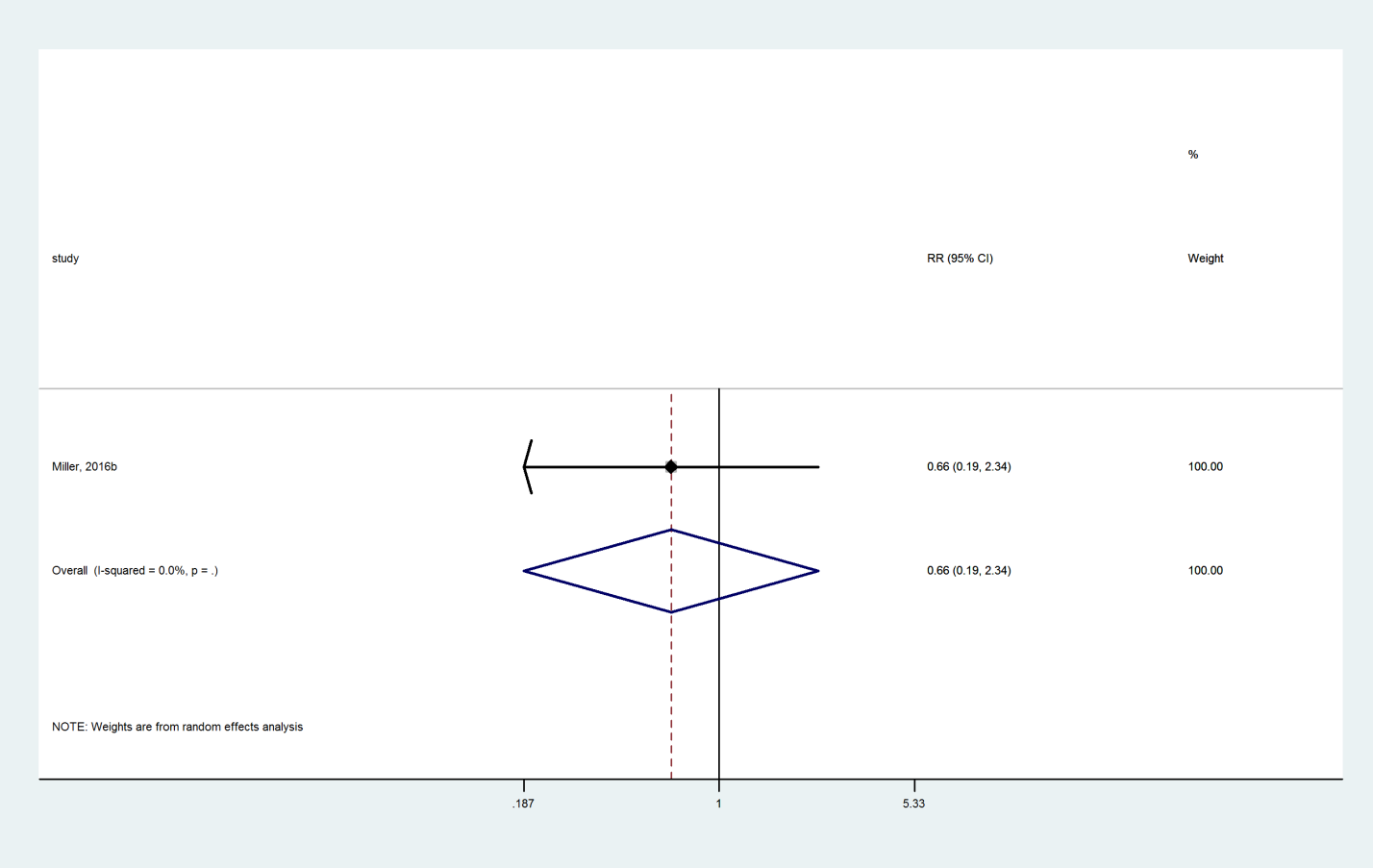
### Vitamin D compared with Calcitonin



### Romosozumab compared with Alendronate



### Abaloparatide compared with Alendronate



# Sensitivity analyses based on dosage and route

## Zoledronate: Nonvertebral Fracture

### Zoledronate compared with Placebo using 5 mg single dose

Y:\TES osteoporosis in women\SR in efficacy\6. Analysis\Direct and Indirect with STATA\2017-08\Direct\trt2_trt1_nonvert_5mg.wmf

### Zoledronate compared with Placebo using other doses

Y:\TES osteoporosis in women\SR in efficacy\6. Analysis\Direct and Indirect with STATA\2017-08\Direct\trt2_trt1_nonvert_otherdose.wmf

## Zoledronate: vertebral fractures

### Zoledronate compared with Placebo using 5 mg single dose

Y:\TES osteoporosis in women\SR in efficacy\6. Analysis\Direct and Indirect with STATA\2017-08\Direct\trt2_trt1_vert_5mg.wmf

## Calcitonin: Vertebral Fracture

### Calcitonin compared with Placebo using the intranasal route

Y:\TES osteoporosis in women\SR in efficacy\6. Analysis\Direct and Indirect with STATA\2017-08\Direct\trt2_trt1_intranasal.wmf

### Calcitonin compared with Placebo using the injectable route

Y:\TES osteoporosis in women\SR in efficacy\6. Analysis\Direct and Indirect with STATA\2017-08\Direct\trt2_trt1_nvert_intran_inject.wmf

### Calcitonin compared with Placebo using the oral route

Y:\TES osteoporosis in women\SR in efficacy\6. Analysis\Direct and Indirect with STATA\2017-08\Direct\trt2_trt1_oral.wmf

# Search strategies

|  |  |  |  |
| --- | --- | --- | --- |
| **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present | | | |
| 1 | exp osteoporosis/ or osteopenia/ or osteoporo\*.mp. or osteopeni\*.mp. or osteopaen\*.mp. or fragil\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |  |  |
| 2 | exp fractures, bone/ |  |  |
| 3 | 1 and 2 |  |  |
| 4 | exp bone density conservation agents/ or exp calcium/ or exp selective estrogen receptor modulators/ or exp vitamin d/ |  |  |
| 5 | (alendronate or etidronate).mp. or ibandronate/ or pamidronate.mp. or residronate.mp. or zolendronate.mp. or bisphosphonate.mp. or disphosphonate.mp. or calcitonin.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |  |  |
| 6 | (raloxifen\* or tamoxifen\* or teriparatide or abaloparatide or romosozumab or bazedoxifene or lasofoxifene or denosumab or pth).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |  |  |
| 7 | randomized controlled trial.pt. |  |  |
| 8 | controlled clinical trial.pt. |  |  |
| 9 | randomized controlled trials/ |  |  |
| 10 | random allocation.sh. |  |  |
| 11 | double blind method.sh. |  |  |
| 12 | single-blind method.sh. |  |  |
| 13 | clinical trial$.pt. |  |  |
| 14 | exp clinical trials/ |  |  |
| 15 | (clinic$ adj25 trial$1).ti,ab. |  |  |
| 16 | ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab. |  |  |
| 17 | placebos.sh. or placebo$.ti,ab. |  |  |
| 18 | random$.ti,ab. |  |  |
| 19 | research design.sh. |  |  |
| 20 | exp evaluation studies/ |  |  |
| 21 | follow up studies.sh. |  |  |
| 22 | prospective studies.sh. |  |  |
| 23 | or/7-22 |  |  |
| 24 | 3 and (4 or 5 or 6) |  |  |
| 25 | 2 and bone density/de and (4 or 5 or 6) |  |  |
| 26 | 24 or 25 |  |  |
| 27 | 26 and ((placebo\* or systematic\*).mp. or comparative study/) [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |  |  |
| 28 | 26 and 23 |  |  |
| 29 | 27 or 28 |  |  |
| 30 | exp Menopause/ |  |  |
| 31 | limit 29 to (("all aged (65 and over)" or "aged (80 and over)") and female) |  |  |
| 32 | 29 and 30 |  |  |
| 33 | 31 or 32 |  |  |
| 34 | osteoporotic fractures/ and (4 or 5 or 6) and 23 |  |  |
| 35 | 33 or 34 |  |  |
| 36 | limit 35 to yr="2012 - 2015" |  |  |
| 37 | ..l/ 35 yr="2011" |  |  |
| 38 | 36 or 37 |  |  |
| 39 | 38 and (2012\* or 2013\* or 2014\* or 2015).em. |  |  |

4 duplicates removed

|  |  |  |  |
| --- | --- | --- | --- |
| **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present | | | |
| 1 | exp osteoporosis/ or osteopenia/ or osteoporo\*.mp. or osteopeni\*.mp. or osteopaen\*.mp. or fragil\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |  |  |
| 2 | exp fractures, bone/ |  |  |
| 3 | randomized controlled trial.pt. |  |  |
| 4 | controlled clinical trial.pt. |  |  |
| 5 | randomized controlled trials/ |  |  |
| 6 | random allocation.sh. |  |  |
| 7 | double blind method.sh. |  |  |
| 8 | single-blind method.sh. |  |  |
| 9 | clinical trial$.pt. |  |  |
| 10 | exp clinical trials/ |  |  |
| 11 | (clinic$ adj25 trial$1).ti,ab. |  |  |
| 12 | ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab. |  |  |
| 13 | placebos.sh. or placebo$.ti,ab. |  |  |
| 14 | random$.ti,ab. |  |  |
| 15 | research design.sh. |  |  |
| 16 | exp evaluation studies/ |  |  |
| 17 | follow up studies.sh. |  |  |
| 18 | prospective studies.sh. |  |  |
| 19 | or/3-18 |  |  |
| 20 | exp Menopause/ |  |  |
| 21 | (1 and 2) or osteoporotic fractures/ |  |  |
| 22 | exp Calcium Compounds/ |  |  |
| 23 | exp Vitamin D/ |  |  |
| 24 | Calcitonin/ |  |  |
| 25 | exp Estrogens/ |  |  |
| 26 | (bazedoxifene or lasofoxifene or tibolone).mp. or parathyroid hormone/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |  |  |
| 27 | strontium ranelate.mp. |  |  |
| 28 | 21 and (22 or 23 or 24 or 25 or 26 or 27) |  |  |
| 29 | exp menopause/ |  |  |
| 30 | 28 and 29 |  |  |
| 31 | limit 28 to (("all aged (65 and over)" or "aged (80 and over)") and female) |  |  |
| 32 | 30 or 31 |  |  |
| 33 | 19 and 32 |  |  |
| 34 | limit 33 to yr="2004 - 2015" |  |  |
| 35 | exp hormone replacement therapy/ and 21 |  |  |
| 36 | 29 and 35 |  |  |
| 37 | limit 35 to (("all aged (65 and over)" or "aged (80 and over)") and female) |  |  |
| 38 | 19 and (36 or 37) |  |  |
| 39 | limit 38 to yr="2004 - 2015" |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| **Embase** 1988 to 2015 Week 12 | | | |
| 1 | fragility fracture/ |  |  |
| 2 | osteoporosis/ or involutional osteoporosis/ or postmenopause osteoporosis/ or primary osteoporosis/ or secondary osteoporosis/ or senile osteoporosis/ |  |  |
| 3 | exp fracture/ |  |  |
| 4 | (2 or metabolic bone disease/) and 3 |  |  |
| 5 | 1 or 4 |  |  |
| 6 | exp bisphosphonic acid derivative/ |  |  |
| 7 | exp selective estrogen receptor modulator/ |  |  |
| 8 | denosumab/ |  |  |
| 9 | "parathyroid hormone[1-34]"/ |  |  |
| 10 | hormone substitution/ or estrogen therapy/ |  |  |
| 11 | exp estrogen/ |  |  |
| 12 | exp calcitonin/ |  |  |
| 13 | bazedoxifene/ |  |  |
| 14 | lasofoxifene/ |  |  |
| 15 | strontium ranelate/ |  |  |
| 16 | tibolone/ |  |  |
| 17 | 6 or 7 or 8 or 9 or 10 or 11 or 12 |  |  |
| 18 | 5 and 17 and (randomized controlled trial/ or meta-analysis/ or systematic review/ or random\*.mp.) [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] |  |  |
| 19 | menopause/ or postmenopause/ |  |  |
| 20 | 18 and 19 and female/ |  |  |
| 21 | ..l/ 20 yr=2011-2015 |  |  |
| 22 | 21 and (201148\* or 2012\* or 2013\* or 2014\* or 2015).em. |  |  |
| 23 | exp calcium/ or exp vitamin d/ or calcium intake/ |  |  |
| 24 | 12 or 23 |  |  |
| 25 | 19 and 24 and (randomized controlled trial/ or random\*.mp. or meta-analysis/ or systematic review/) [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] |  |  |
| 26 | 5 and 25 and female/ |  |  |
| 27 | limit 26 to yr="2007 - 2015" |  |  |
| 28 | 27 and (200736\* or 200737\* or 200738\* or 200739\* or 20074\* or 20075\* or 2008\* or 2009\* or 201\*).em. |  |  |
| 29 | 12 or 13 or 14 or 15 or 16 |  |  |
| 30 | 5 and 29 and (randomized controlled trial/ or random\*.mp. or meta-analysis/ or systematic review/) [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] |  |  |
| 31 | 30 and 19 |  |  |
| 32 | 31 and female/ |  |  |
| 33 | ..l/ 32 yr=2004-2015 |  |  |
| 34 | 22 or 28 or 33 |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| **#** | **Query** | **Limiters/Expanders** | **Last Run Via** |
| S21 | S3 AND S11 AND S20 | Limiters - Published Date: 20040101-20150317 Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S20 | S18 OR S19 | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S19 | (MH "Parathyroid Hormones+") OR (MH "Teriparatide") | Limiters - Published Date: 20070801-20150317 Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S18 | "strontium ranelate" | Limiters - Published Date: 20070801-20150317 Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S17 | S3 AND S11 AND S16 | Limiters - Published Date: 20070801-20150317 Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S16 | S13 OR S14 OR S15 | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S15 | (MH "Calcitonin") | Limiters - Published Date: 20111101-20150317 Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S14 | (MH "Calcium") OR (MH "Calcium, Dietary") | Limiters - Published Date: 20111101-20150317 Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S13 | (MH "Vitamin D+") OR (MH "Ergocalciferols") OR (MH "Cholecalciferol") OR (MH "Calcitriol") | Limiters - Published Date: 20111101-20150317 Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S12 | S10 AND S11 | Limiters - Published Date: 20111101-20150317 Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S11 | (MH "Menopause+") OR (MH "Postmenopause") OR (MH "Postmenopausal Disorders") | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S10 | S3 AND S9 | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S9 | S4 OR S5 OR S6 OR S7 OR S8 | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S8 | (MH "Hormone Replacement Therapy+") OR (MH "Estrogens+") OR (MH "Estrogens, Conjugated") | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S7 | "denosumab" | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S6 | (MH "Teriparatide") | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S5 | (MH "Selective Estrogen Receptor Modulators+") | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S4 | (MH "Diphosphonates+") | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S3 | S1 AND S2 | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S2 | (MH "Fractures+") | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |
| S1 | (MH "Osteoporosis+") | Search modes - Boolean/Phrase | Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL with Full Text |

Web of Science

(osteoporo\* OR “bone density” OR “bone loss” OR osteopaen\* OR osteopenia\* OR bmd OR “bone mineral density” OR fragility) AND fractur\* AND (elderly OR menopaus\* OR postmenopaus\*) AND (randomized OR randomized OR RCT\* OR meta-analysis OR systematic\*)

AND

(bisphosphon\* OR diphosphon\* OR alendron\* OR etidron\* OR ibandron\* OR pamidronat\* OR residronat\* OR zolendron\* OR SERMS OR raloxifen\* OR tamoxifen\* OR denosumab OR estrogen\* OR oestrogen\*) Limit to 2012-2015

OR

(“vitamin d\*” OR dihydrotachysterol OR calcitriol OR cholecalciferol OR colecalciferol OR alfacalcidol OR hydroxyvitamin\* OR dihydroxyvitamin\*) Limit to 2007-2015

OR

(bazedoxifen\* OR lasofoxafen\* OR pth OR “parathyroid hormone” OR “1-84” OR “1-48” OR teriparatide OR “strontium ranulate”) Limit to 2004-2015

2017 update

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>**   |  |  |  |  | | --- | --- | --- | --- | |  |  |  |  | | 1 exp osteoporosis/ or osteopenia/ or osteoporo\*.mp. or osteopeni\*.mp. or osteopaen  \*.mp. or fragil\*.mp. | | | | | | |  | | 2 | exp fractures, bone/ |  |  |  |  |  | | 3 | 1 and 2 |  |  |  |  |  | | 4 | exp bone density conservation agents/ or exp calcium/ or exp selective estrogen receptor modulators/ or exp vitamin d/ |  |  |  |  |  | | 5 | (alendronate or etidronate).mp. or ibandronate/ or pamidronate.mp. or residronate.mp. or zolendronate.mp. or bisphosphonate.mp. or disphosphonate.mp. or calcitonin.mp. |  |  |  |  |  | | 6 | (raloxifen\* or tamoxifen\* or teriparatide or bazedoxifene or lasofoxifene or denosumab or pth).mp. |  |  |  |  |  | | 7 | randomized controlled trial.pt. |  |  |  |  |  | | 8 | controlled clinical trial.pt. |  |  |  |  |  | | 9 | randomized controlled trials/ |  |  |  |  |  | | 10 | random allocation.sh. |  |  |  |  |  | | 11 | double blind method.sh. |  |  |  |  |  | | 12 | single-blind method.sh. |  |  |  |  |  | | 13 | clinical trial$.pt. |  |  |  |  |  | | 14 | (clinic$ adj25 trial$1).ti,ab. |  |  |  |  |  | | 15 | ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab. |  |  |  |  |  | | 16 | placebos.sh. or placebo$.ti,ab. |  |  |  |  |  | | 17 | random$.ti,ab. |  |  |  |  |  | | 18 | research design.sh. |  |  |  |  |  | | 19 | exp evaluation studies/ |  |  |  |  |  | | 20 | follow up studies.sh. |  |  |  |  |  | | 21 | prospective studies.sh. |  |  |  |  |  | | 22 | or/7-21 |  |  |  |  |  | | 23 | 3 and (4 or 5 or 6) |  |  |  |  |  | | 24 | 2 and bone density/de and (4 or 5 or 6) |  |  |  |  |  | | 25 | 23 or 24 |  |  |  |  |  | | 26 | 25 and ((placebo\* or systematic\*).mp. or comparative study/) |  |  |  |  |  | | 27 | 22 and 25 |  |  |  |  |  | | 28 | 26 or 27 |  |  |  |  |  | | 29 | exp menopause/ |  |  |  |  |  | | 30 | limit 28 to (("all aged (65 and over)" or "aged (80 and over)") and female) |  |  |  |  |  | | 31 | 28 and 29 |  |  |  |  |  | | 32 | 30 or 31 |  |  |  |  |  | | 33 | osteoporotic fractures/ and (4 or 5 or 6) and 22 |  |  |  |  |  | | 34 | 32 or 33 |  |  |  |  |  | | 35 | 34 and (201504\* or 201505\* or 201506\* or 201507\* or 201508\* or 201509\* or 20151\* or 2016\* or 2017\*).dc. |  |  |  |  |  | | 36 | remove duplicates from 35 |  |  |  |  |  | |  |  |  |  |  |  |  | |

CENTRAL 44 same as above strategy

**Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
| 1 | exp osteoporosis/ or osteopenia/ or osteoporo\*.mp. or osteopeni\*.mp. or osteopaen\*.mp. or fragil\*.mp. |  |  |  |  |  |
| 2 | exp fractures, bone/ |  |  |  |  |  |
| 3 | randomized controlled trial.pt. |  |  |  |  |  |
| 4 | controlled clinical trial.pt. |  |  |  |  |  |
| 5 | randomized controlled trials/ |  |  |  |  |  |
| 6 | random allocation.sh. |  |  |  |  |  |
| 7 | double blind method.sh. |  |  |  |  |  |
| 8 | single-blind method.sh. |  |  |  |  |  |
| 9 | clinical trial$.pt. |  |  |  |  |  |
| 10 | (clinic$ adj25 trial$1).ti,ab. |  |  |  |  |  |
| 11 | ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab. |  |  |  |  |  |
| 12 | placebos.sh. or placebo$.ti,ab. |  |  |  |  |  |
| 13 | random$.ti,ab. |  |  |  |  |  |
| 14 | research design.sh. |  |  |  |  |  |
| 15 | exp evaluation studies/ | 234194 | Advanced |  |  |  |
| 16 | follow up studies.sh. | 593252 | Advanced |  |  |  |
| 17 | prospective studies.sh. | 464599 | Advanced |  |  |  |
| 18 | or/3-17 | 2758673 | Advanced |  |  |  |
| 19 | exp menopause/ or menopaus\*.mp. or postmenopaus\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] | 101127 | Advanced |  |  |  |
| 20 | (1 and 2) or osteoporotic fractures/ | 21321 | Advanced |  |  |  |
| 21 | exp calcium compounds/ | 69384 | Advanced |  |  |  |
| 22 | exp vitamin d/ | 52571 | Advanced |  |  |  |
| 23 | calcitonin/ | 15364 | Advanced |  |  |  |
| 24 | exp estrogens/ | 155934 | Advanced |  |  |  |
| 25 | (bazedoxifene or lasofoxifene or tibolone).mp. or parathyroid hormone/ | 28414 | Advanced |  |  |  |
| 26 | strontium ranelate.mp. | 739 | Advanced |  |  |  |
| 27 | 20 and (21 or 22 or 23 or 24 or 25 or 26 or ex hormone replacement therapy/) | 2990 | Advanced |  |  |  |
| 28 | ((vitamin adj1 d\*) or calcitonin\* or estrogen\* or oestrogen\* or estradiol\* or oestradiol\* or calcium\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] | 868766 | Advanced |  |  |  |
| 29 | 20 and 28 | 4957 | Advanced |  |  |  |
| 30 | 27 or 29 | 5294 | Advanced |  |  |  |
| 31 | 19 and 30 | 2370 | Advanced |  |  |  |
| 32 | limit 30 to (("all aged (65 and over)" or "aged (80 and over)") and female) | 2466 | Advanced |  |  |  |
| 33 | (31 or 32) and 18 | 1344 | Advanced |  |  |  |
| 34 | 33 and (201504\* or 201505\* or 201506\* or 201507\* or 201508\* or 201509\* or 20151\* or 2016\* or 2017\*).dc. | 87 | Advanced |  |  |  |
| 35 | remove duplicates from 34 | 70 |  |  |  |  |

CENTRAL 26, strategy same as above.

**Embase <1988 to 2017 Week 27>**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
| 1 | fragility fracture/ |  |  |  |  |  |
| 2 | osteoporosis/ or involutional osteoporosis/ or postmenopause osteoporosis/ or primary osteoporosis/ or secondary osteoporosis/ or senile osteoporosis/ |  |  |  |  |  |
| 3 | exp fracture/ |  |  |  |  |  |
| 4 | (2 or metabolic bone disease/) and 3 |  |  |  |  |  |
| 5 | 1 or 4 |  |  |  |  |  |
| 6 | exp bisphosphonic acid derivative/ |  |  |  |  |  |
| 7 | exp selective estrogen receptor modulator/ |  |  |  |  |  |
| 8 | denosumab/ |  |  |  |  |  |
| 9 | "parathyroid hormone[1-34]"/ |  |  |  |  |  |
| 10 | hormone substitution/ or estrogen therapy/ |  |  |  |  |  |
| 11 | hormone substitution/ or estrogen therapy/ |  |  |  |  |  |
| 12 | exp calcitonin/ |  |  |  |  |  |
| 13 | bazedoxifene/ |  |  |  |  |  |
| 14 | lasofoxifene/ |  |  |  |  |  |
| 15 | strontium ranelate/ |  |  |  |  |  |
| 16 | tibolone/ |  |  |  |  |  |
| 17 | or/6-16 |  |  |  |  |  |
| 18 | 5 and 17 and (randomized controlled trial/ or meta-analysis/ or systematic review/ or random\*.mp.) |  |  |  |  |  |
| 19 | menopause/ or postmenopause/ |  |  |  |  |  |
| 20 | 18 and (19 or female/) |  |  |  |  |  |
| 21 | 20 and (201504\* or 201505\* or 201506\* or 201507\* or 201508\* or 201509\* or 20151\* or 2016\* or 2017\*).dc. |  |  |  |  |  |
| 22 | limit 20 to (female and adult <18 to 64 years>) |  |  |  |  |  |
| 23 | 22 and (201504\* or 201505\* or 201506\* or 201507\* or 201508\* or 201509\* or 20151\* or 2016\* or 2017\*).dc. |  |  |  |  |  |
| 24 | 21 or 23 |  |  |  |  |  |
| 25 | remove duplicates from 24 |  |  |  |  |  |

WEB of Science

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| # 6 |  | #5 AND #1  *Indexes=SCI-EXPANDED, ESCI Timespan=2015-2017* |  |  |  |
|  | | | | | |
| # 5 |  | #4 OR #3 OR #2  *Indexes=SCI-EXPANDED, ESCI Timespan=2015-2017* |  |  |  |
|  | | | | | |
| # 4 |  | TS=(bazedoxifen\* OR lasofoxafen\* OR pth OR “parathyroid hormone” OR “1-84” OR “1-48” OR teriparatide OR “strontium ranulate”)  *Indexes=SCI-EXPANDED, ESCI Timespan=2015-2017* |  |  |  |
|  | | | | | |
| # 3 |  | TS=(“vitamin d\*” OR dihydrotachysterol OR calcitriol OR cholecalciferol OR colecalciferol OR alfacalcidol OR hydroxyvitamin\* OR dihydroxyvitamin\*)  *Indexes=SCI-EXPANDED, ESCI Timespan=2015-2017* |  |  |  |
|  | | | | | |
| # 2 |  | TS=(bisphosphon\* OR diphosphon\* OR alendron\* OR etidron\* OR ibandron\* OR pamidronat\* OR residronat\* OR zolendron\* OR SERMS OR raloxifen\* OR tamoxifen\* OR denosumab OR estrogen\* OR oestrogen\*)  *Indexes=SCI-EXPANDED, ESCI Timespan=2015-2017* |  |  |  |
|  | | | | | |
| # 1 |  | TS=((osteoporo\* OR bone density OR bone loss OR osteopaen\* OR osteopenia\* OR bmd OR bone mineral density OR fragility) AND fractur\* AND (elderly OR menopaus\* OR postmenopaus\*) AND (randomized OR randomized OR RCT\* OR meta-analysis OR systematic\*))  *Indexes=SCI-EXPANDED, ESCI Timespan=2015-2017* |  |  |  |

CINAHL

|  |  |
| --- | --- |
| **#** | **Query** |
| S23 | S12 OR S17 OR S21 |
| S22 | S12 OR S17 OR S21 |
| S21 | S3 AND S11 AND S20 |
| S20 | S18 OR S19 |
| S19 | (MH "Parathyroid Hormones+") OR (MH "Teriparatide") |
| S18 | "strontium ranelate" |
| S17 | S3 AND S11 AND S16 |
| S16 | S13 OR S14 OR S15 |
| S15 | (MH "Calcitonin") |
| S14 | (MH "Calcium") OR (MH "Calcium, Dietary") |
| S13 | (MH "Vitamin D+") OR (MH "Ergocalciferols") OR (MH "Cholecalciferol") OR (MH "Calcitriol") |
| S12 | S10 AND S11 |
| S11 | (MH "Menopause+") OR (MH "Postmenopause") OR (MH "Postmenopausal Disorders") |
| S10 | S3 AND S9 |
| S9 | S4 OR S5 OR S6 OR S7 OR S8 |
| S8 | (MH "Hormone Replacement Therapy+") OR (MH "Estrogens+") OR (MH "Estrogens, Conjugated") |
| S7 | "denosumab" |
| S6 | (MH "Teriparatide") |
| S5 | (MH "Selective Estrogen Receptor Modulators+") |
| S4 | (MH "Diphosphonates+") |
| S3 | S1 AND S2 |
| S2 | (MH "Fractures+") |
| S1 | (MH "Osteoporosis+") |