

**Table 2.** Clinical trials on vitamin D intervention in Type 2 diabetes mellitus

S. No	Year	Country	Participants (Number of participants)	Age	Vitamin D form and dose intervention	Study duration	Out come	Reference
<b>Positive out comes</b>								
1	2012	USA	Overweight or obese African-Americans with prediabetes or early diabetes (n=89)		4000 IU/day vitamin D <sub>3</sub>	12 weeks	1. Insulin sensitivity decreased by 4% in the vitamin D group (12% increase in the placebo) (p = 0.034). 2. Insulin secretion increased by 12% in the vitamin D group (2% increase in the placebo) (p = 0.024)	Harris SS et al <sup>80</sup>
2	2011	Iran	Type 2 diabetes mellitus (n=72)	30-75	Calcitriol 0.25 µg per day	12 weeks	Insulin secretion (HOMA-%β) unchanged in the control group, it increased in the treatment group (p=0.009)	Eftekhari MH et al <sup>81</sup>
3	2011	USA	Adults at high risk of diabetes (n=92)	mean 57	Cholecalciferol 2000 IU/daily or calcium carbonate 400 mg twice daily	16 weeks	Disposition index (DI) increased in vitamin D group and decreased in no-vitamin D group (adjusted mean change ± SE: 300 ± 130 compared with -126 ± 127, respectively; P = 0.011) Improvement in insulin secretion (62 ± 39 compared with -36 ± 37 mU · L(-1) · min, respectively; P = 0.046)	Mitri J et al <sup>82</sup>
4	2011	Iran	Type 2 diabetes mellitus (n=90)	30-60	3 groups: 1. consume plain yogurt drink (PY- no vitamin D and 150 mg Ca/250 mL); 2. vitamin D-fortified yogurt drink (DY; 500 IU vitamin D <sub>3</sub> and 150 mg Ca/250 mL); 3. vitamin D + calcium-fortified yogurt drink (DCY; 500 IU vitamin D <sub>3</sub> and 250 mg Ca/250 mL)	12 weeks	DY and DCY groups HOMA-IR [-0.6 ± 1.4 (P = 0.001) and -0.6 ± 3.2 (P <0.001)] decreased significantly more than in the PY group	Nikooyeh B et al <sup>83</sup>
5	2010	UK	South Asians with T2DM and vitamin D inadequacy (n=52)	33-72	400 IU of vitamin D <sub>3</sub> and 1200 mg of calcium carbonate/day	16-24 weeks	Reduction in HbA1C levels post treatment	Sabherwal S et al <sup>84</sup>

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6	2009	New Zealand	Vitamin D deficient Subjects =42 Placebo =39	41.8+10.1 41.5+9.1	4000 IU Cholecalciferol/day	6 months	Significant improvement in insulin secretion (P<0.003) and insulin resistance (P<0.02) compared to placebo	Von Hurst PR et al <sup>85</sup>
7	2008	USA	Nurses' Health Study (n=83,779)	46	A combined daily intake of >1,200 mg/day calcium and >800 IU vitamin D/day compared with an intake of <600 mg and 400 IU calcium and vitamin D	20 years	33% lower risk of type 2 diabetes with RR of 0.67 (0.49–0.90)	Pittas AG et al <sup>70</sup>
8	2007	USA	Caucasian adults without diabetes (n=314)	> or =65	500 mg calcium citrate and 700 IU vitamin D(3) or placebos daily	3 years	Improved HOMA-IR in subjects with IFG	Pittas AG et al <sup>86</sup>
9	2005	USA	Women's Health Study cohort (10,066 participating in the Women's Health Study analyzed)	>45	Multiple logistic regression models to estimate multivariable odds ratios (ORs) and 95% CIs comparing different dietary intake levels of calcium and vitamin D.	Data analysis	Intakes of calcium and dairy products may be associated with lower prevalence of the metabolic syndrome in middle-aged and older women	Liu S et al <sup>77</sup>
10	2003	Bulgaria	Type 2 diabetes mellitus (n=10)		Treated with cholecalciferol 1332 IU daily for one month	4 weeks	First (FPIS) and second (SPIS) phases of insulin secretion studied by IVGTT. FPIS increased significantly by 34.3%; SPIS by 20.4% (p >0.8 NS). Correlation between the change in FPIS and the change in 25(OH) D level after supplementation (p <0.018)	Borissova AM et al <sup>87</sup>
11	1995	UK	Asians – glucose intolerant (n=22)	44.9	Cholecalciferol 100,000 IU/ stat	8-12 weeks after follow-up	Increase in post OGTT insulin and C-peptide levels	Boucher BJ et al <sup>88</sup>
12	1994	USA	T2DM subjects (n=35)	61	1 µg/day of 1,25 (OH) <sub>2</sub> D <sub>3</sub> Vs placebo	4 days	Tendency towards better insulin secretion	Orwoll E et al <sup>89</sup>
13	1986	Japan	Type 2 DM subjects (n=14)	54.3	Alphacalcidol 2 µg/day Vs placebo	3 weeks	Improved insulin secretion	Inomata S et al <sup>90</sup>
14	1986	Turkey	Vitamin D deficient women (n=4)	32.7	Cholecalciferol 2000 IU/day oral	6 months	Increased insulinogenic index	Gedik O et al <sup>91</sup>

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15	1986	Belgium	Subjects with epilepsy (n=10); elderly subjects (n=15)	Mean 56 and 78 in two groups	25 OH D – loading dose 200 µg and daily 10 µg/day	2 weeks	In epilepsy subjects only - with decrease in fasting insulin and post challenge insulin by OGTT	Nyomba BL et al <sup>92</sup>
<b>Negative out comes</b>								
1	2010	UK	Type 2 diabetics (n=61)	65	Vitamin D <sub>3</sub> 100,000 IU once orally Vs 200,000 IU once orally	16 weeks	No change in HbA1c, FPG and IR HOMA	Witham MD et al <sup>93</sup>
2	2010	Norway	Non-diabetic overweight/obese individuals (n=438)	38 (21-70)	Vitamin D <sub>3</sub> 40,000 IU/week Vs 20,000 IU/week Vs placebo. All received 500 mg of calcium/day	1 year	No change in HbA1c (P=NS), FPG pr 2hr PG (P=NS), IR HOMA (P=NS) and QUICKI (P=NS)	Jorde R et al <sup>94</sup>
3	2010	USA	Type 2 diabetes mellitus Group-1 (13) Group-2 (11)	61+4 54+3	Subjects randomized to receive 400 IU (Group 1) or 1200 IU (Group 2) cholecalciferol for 4 months	16 weeks	No significant differences were noted in fasting plasma glucose, HbA1c, QUICKI	Patel P et al <sup>95</sup>
4	2010	India	Type 2 diabetes mellitus (n=28)	42-45	300,000 IU of vitamin D <sub>3</sub> administered intramuscularly - vitamin D treated group (group D) or a placebo group (group P)	4 weeks	No significant differences were found between the groups at baseline and four weeks with respect to serum fasting plasma glucose and serum insulin, post OGTT plasma glucose and serum insulin levels, and HOMA-IR	Parekh D et al <sup>96</sup>
5	2009	UK	Recent previous osteoporotic fracture (n=5292)	77	Factorial design to oral 800 IU daily vitamin D <sub>3</sub> , 1000 mg calcium (CaCO <sub>3</sub> ), both, or placebo	24–62 months	No evidence that vitamin D <sub>3</sub> alone or in combination with calcium was able to prevent the development of diabetes	Avenell A et al <sup>97</sup>
6	2009	Norway	Type 2 diabetes mellitus (n=36)	21-75	On metformin and bed-time insulin, were randomized to supplementation with cholecalciferol (40,000 IU per week) versus placebo	6 months	Fasting glucose, insulin, C-peptide, levels not significantly different from baseline	Jorde R et al <sup>98</sup>
7	2009	India	Healthy, middle-aged, centrally obese men (n=100)	> or = 35	Three doses of vitamin D <sub>3</sub> (120,000 IU each; supplemented group) fortnightly or placebo (control group)	6 weeks	No changes in insulin secretion, basal indices of insulin sensitivity with supplementation	Nagpal J et al <sup>99</sup>

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S. No	Year	Country	Participants (Number of participants)	Age	Vitamin D form and dose intervention	Study duration	Out come	Reference
8	2009	Germany	Healthy individuals (mean 25 OHD levels <12 ng/ml) (n=200)	48 (18-70)	Placebo Vs vitamin D <sub>3</sub> 3332 IU/day	1 year	No change in HbA1C (P=0.90) and FPG (P=0.39)	Zitterman A et al <sup>100</sup>
9	2008	USA	Healthy postmenopausal women (n=33,951)	50-79	Double-blind randomized fashion -1,000 mg elemental calcium plus 400 IU vitamin D <sub>3</sub> daily, or placebo	7 years	Calcium plus vitamin D <sub>3</sub> supplementation did not reduce the risk of developing diabetes over 7 years of follow-up	de Boer IH et al <sup>101</sup>
10	2008	Australia	Adults with vitamin D insufficiency (25OH D levels < or = 50 nmol/L) and without diabetes (12 with impaired glucose tolerance) (n=33)		Two oral doses of 100 000 IU of cholecalciferol, 2 wk apart	4 weeks	No change in blood glucose or insulin mean of 0-120 concentrations, no change in insulin sensitivity (Avignon's insulin sensitivity index) [SiM], QUICKI, HOMA after vitamin D treatment	Tai K <sup>102</sup>
11	2008	UK	Stable type 2 DM (n=53)	64	Vitamin D <sub>2</sub> 100,000 IU once (n=17) Vs placebo (n=17)	8 weeks	No change in HbA1C (P=0.74) or IR HOMA (P=0.72) If 25 OHD rise >5 ng/ml IR HOMA significantly improved	Sugden JA et al <sup>103</sup>
12	1997	Germany	Healthy males (n=18)	26	1.5 µg/day of 1,25 (OH) <sub>2</sub> D <sub>3</sub> Vs placebo	7 days	No change in insulin sensitivity	Fliser D et al <sup>104</sup>
13	1990	Czechoslovakia	Ethnicity not reported (n=13)	33.4	3 µg/day of 1,25 (OH) <sub>2</sub> D <sub>3</sub>	4 days	No change in insulin secretion	Zofkova I & Stobla P <sup>105</sup>
14	1989	Denmark	Men with impaired glucose tolerance (n=14)	60-63	Alphacalcidol 2 µg/day	18 months	No change in insulin sensitivity	Lind L et al <sup>106</sup>
15	1987	Sweden	Caucasian men with IGT and vitamin D sufficient (n=65) Vs	61-65	Alphacalcidol 0.75 µg/day Vs placebo	3 months	No change in insulin sensitivity	Ljunghall S et al <sup>107</sup>
16	1984	Denmark	Postmenopausal women (n=151)	45-54	Placebo Vs vitamin D <sub>2</sub> 2000 IU/ day, calcium 500 mg/day to all	2 years	No change in FPG (P=NS)	Nilas L, Christiansen C <sup>108</sup>