

## Supplement 1: Search Strategy

### MEDLINE

Database: Ovid MEDLINE(R) ALL <1946 to January 17, 2020>

Search Strategy:

- 
- 1 exp Vitamin D/ (57819)
  - 2 (Cholecalciferol\* or calciol or HYDROXYCHOLECALCIFEROL\* or hydroxyvitamins d or CALCIFEDIOL or 25 hydroxyvitamin d3 or 25-hydroxycholecalciferol or calcidiol or DIHYDROXYCHOLECALCIFEROL\* or dihydroxyvitamins d or CALCITRIOL or 1 alpha,25 dihydroxyvitamin d3 or 1 alpha,25-dihydroxycholecalciferol or 1,25-dihydroxyvitamin d3 or ergocalciferol\* or Dihydrotachysterol or 25-Hydroxyvitamin D 2).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (38570)
  - 3 (vitamin adj (d or d2 or d3 or d-2 or d-3)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (75439)
  - 4 Vitamin D Deficiency/ (15265)
  - 5 1 or 2 or 3 or 4 (87829)
  - 6 exp Hypertension/ (250658)
  - 7 hypertensi\*.mp. (499579)
  - 8 ((increase or elevat\* or high\*) adj2 blood adj1 pressure).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (38782)
  - 9 ((systolic or diastolic or arterial) adj3 pressure).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (179307)
  - 10 7 or 8 or 9 (627657)
  - 11 adolescent/ or exp child/ (2958419)
  - 12 (child or children or childhood or youth or teenage\* or p?ediatric\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (2477749)
  - 13 (adolescen\* or (school adj age) or youngster\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (2066781)
  - 14 11 or 12 or 13 (3499936)
  - 15 5 and 10 and 14 (324)
  - 16 5 and 10 (2408)
  - 17 limit 16 to "all child (0 to 18 years)" (259)
  - 18 15 or 17 (349)
  - 19 (pediatric? or child or children or adolescen\* or youth).jw. (542548)
  - 20 16 and 19 (58)
  - 21 18 or 20 (353)

## **EMBASE**

Database: Embase Classic <1947 to 1973>, Embase <1974 to 2020 January 17>

Search Strategy:

- 
- 1 exp vitamin D/ (140645)
  - 2 exp vitamin D deficiency/ (28964)
  - 3 (Cholecalciferol\* or calciol or HYDROXYCHOLECALCIFEROL\* or hydroxyvitamins d or CALCIFEDIOL or 25 hydroxyvitamin d3 or 25-hydroxycholecalciferol or calcidiol or DIHYDROXYCHOLECALCIFEROL\* or dihydroxyvitamins d or CALCITRIOL or 1 alpha,25 dihydroxyvitamin d3 or 1 alpha,25-dihydroxycholecalciferol or 1,25-dihydroxyvitamin d3 or ergocalciferol\* or Dihydrotachysterol or 25-Hydroxyvitamin D 2).mp. (52332)
  - 4 (vitamin adj (d or d2 or d3 or d-2 or d-3)).mp. (130950)
  - 5 1 or 2 or 3 or 4 (162755)
  - 6 exp hypertension/ (733633)
  - 7 hypertensi\*.mp. (938420)
  - 8 ((increase or elevat\* or high\*) adj2 blood adj1 pressure).mp. (58276)
  - 9 ((systolic or diastolic or arterial) adj3 pressure).mp. (355528)
  - 10 6 or 7 or 8 or 9 (1221108)
  - 11 child/ (1769502)
  - 12 exp adolescent/ (1484727)
  - 13 (child or children or childhood or youth or teenage\* or p?ediatric\*).mp. (2867838)
  - 14 (adolescen\* or (school adj age) or youngster\*).mp. (1596691)
  - 15 11 or 12 or 13 or 14 (3542372)
  - 16 5 and 10 and 15 (1398)
  - 17 5 and 10 (10579)
  - 18 limit 17 to child <unspecified age> (646)
  - 19 16 or 18 (1398)

**CINAHL**

#	Query	Limiters/Expanders	Results
S17	S14 OR S16	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	83
S16	S5 AND S9	Expanders - Apply equivalent subjects Narrow by SubjectAge: - all child Search modes - Boolean/Phrase	71
S15	S5 AND S9	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	463
S14	S5 AND S9 AND S13	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	83
S13	S10 OR S11 OR S12	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	961,298
S12	Ti (youngster or school age or adolescen* or paediatric* or pediatric* or teenage* or youth or child*) or ab (youngster or school age or adolescen* or paediatric* or pediatric* or teenage* or youth or child*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	398,135
S11	(MH "Adolescence+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	477,443
S10	(MH "Child+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	596,921
S9	S6 OR S7 OR S8	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	81,207
S8	ti (high or elevated or increase* or systolic or diastolic or arterial) n3 pressure* or ab (high or elevated or increase* or systolic or diastolic or arterial) n3 pressure*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	5,573
S7	ti hypertensi* or ab hypertensi*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	35,745
S6	(MH "Hypertension+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	69,915
S5	S1 OR S2 OR S3 OR S4	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	20,348
S4	Ti (vitamin d or vitamin d2 or vitamin d3 or vitamin d 3 or vitamin d 2) or ab (vitamin d or vitamin d2 or vitamin d3 or vitamin d 3 or vitamin d 2)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	10,864
S3	Ti (alpha,25-dihydroxycholecalciferol or ergocalciferol* or Dihydrotachysterol or	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	101

	dihydroxyvitamin d or dihydroxyvitamins d or 1 alpha,25 dihydroxyvitamin d3 or 1 alpha,25-dihydroxycholecalciferol or 1,25-dihydroxyvitamin d3 or 25-Hydroxyvitamin D 2) or ab (alpha,25-dihydroxycholecalciferol or ergocalciferol* or Dihydrotachysterol or dihydroxyvitamin d or dihydroxyvitamins d or 1 alpha,25 dihydroxyvitamin d3 or 1 alpha,25-dihydroxycholecalciferol or 1,25-dihydroxyvitamin d3 or 25-Hydroxyvitamin D 2)		
S2	Ti (Cholecalciferol* or calciol or HYDROXYCHOLECALCIFEROL* or CALCIFEDIOL or 25-hydroxycholecalciferol or calcidol or DIHYDROXYCHOLECALCIFEROL* or CALCITRIOL) or ab (Cholecalciferol* or calciol or HYDROXYCHOLECALCIFEROL* or CALCIFEDIOL or 25-hydroxycholecalciferol or calcidol or DIHYDROXYCHOLECALCIFEROL* or CALCITRIOL)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	360
S1	(MH "Vitamin D+") OR (MH "Vitamin D Deficiency+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	18,743

**PUBMED**

Search	Query	Items found
#29	Search (#7 and #17 and #28)	3648
#28	Search (#18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27)	3454758
#27	Search youngster*[tiab]	2476
#26	Search school age[tiab]	13013
#25	Search adolescen*[tiab]	286605
#24	Search paediatric*[tiab]	64591
#23	Search pediatric*[tiab]	289152
#22	Search teenage*[tiab]	20898
#21	Search youth[tiab]	68591
#20	Search ((child[tiab] or children[tiab] or childhood[tiab]))	1333474
#19	Search child[mesh]	1872154
#18	Search adolescent[mesh]	1983762
#17	Search (# 8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16)	4646659
#16	Search (hypertension[tiab] or hypertensive[tiab] or hypertensives[tiab])	426502
#15	Search arterial pressure[tiab]	58738
#14	Search diastolic pressure[tiab]	13643
#13	Search systolic pressure[tiab]	13954
#12	Search increase blood pressure*[tiab]	760
#11	Search elevated blood pressure[tiab]	6289
#10	Search ((systolic blood pressure*[tiab] or diastolic blood pressure*[tiab] or arterial blood pressure*[tiab]))	98847
#9	Search high blood pressure*[tiab]	14672
#8	Search hypertension[mesh]	250320
#7	Search (#1 or #2 or #3 or #4 or #5 or #6)	87699
#6	Search (vitamin d[tiab] or vitamin d2[tiab] or vitamin d3[tiab] or vitamin d 3[tiab] or vitamin d 2[tiab])	66554
#5	Search (dihydroxyvitamin d[tw] or dihydroxyvitamins d[tw] or 1 alpha,25 dihydroxyvitamin d3[tw] or 1 alpha,25-dihydroxycholecalciferol[tw] or 1,25-dihydroxyvitamin d3[tw] or 25-Hydroxyvitamin D 2[tw])	12196
#4	Search 25 hydroxyvitamin d3 [tw]	2989
#3	Search (Cholecalciferol*[tw] or calciol[tw] or HYDROXYCHOLECALCIFEROL*[tw] or CALCIFEDIOL[tw] or 25-hydroxycholecalciferol[tw] or calcidiol[tw] or DIHYDROXYCHOLECALCIFEROL*[tw] or CALCITRIOL[tw] or alpha,25-dihydroxycholecalciferol[tw] or ergocalciferol*[tw] or Dihydrotachysterol[tw])	36629
#2	Search vitamin D deficiency [mesh:noexp]	15220
#1	Search vitamin D [mesh]	57729

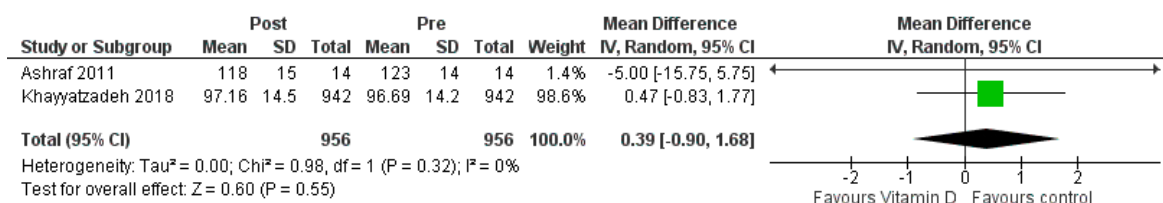
### **Cochrane Library**

#1 MeSH descriptor: [Vitamin D] explode all trees 4778  
#2 MeSH descriptor: [Vitamin D Deficiency] explode all trees 1269  
#3 (Cholecalciferol\* or calciol or HYDROXYCHOLECALCIFEROL\* or CALCIFEDIOL):ti,ab,kw 3039  
#4 (calcidiol or DIHYDROXYCHOLECALCIFEROL\* or CALCITRIOL):ti,ab,kw 1897  
#5 (ergocalciferol\* or Dihydrotachysterol or dihydroxyvitamin d or dihydroxyvitamins d or 1 alpha,25 dihydroxyvitamin d3):ti,ab,kw 1826  
#6 (vitamin d):ti,ab,kw 12995  
#7 (vitamin d2 or vitamin d 3):ti,ab,kw 7528  
#8 #1 or #2 or #3 or #4 or #5 or #6 or #7 14586  
#9 MeSH descriptor: [Hypertension] explode all trees 17001  
#10 (hypertensi\* or (high or elevated or increase\* or systolic or diastolic or arterial) near/3 pressure\*):ti,ab,kw 568810  
#11 #9 or #10 568810  
#12 MeSH descriptor: [Child] explode all trees 1209  
#13 MeSH descriptor: [Adolescent] explode all trees 102003  
#14 (youngster or school age or adolescen\* or paediatric\* or pediatric\* or teenage\* or youth or child\*):ti,ab,kw 243608  
#15 #12 or #13 or #14 243608  
#16 #8 and #11 and #15 1559  
1525 Trials matching "#16 - #8 and #11 and #15"

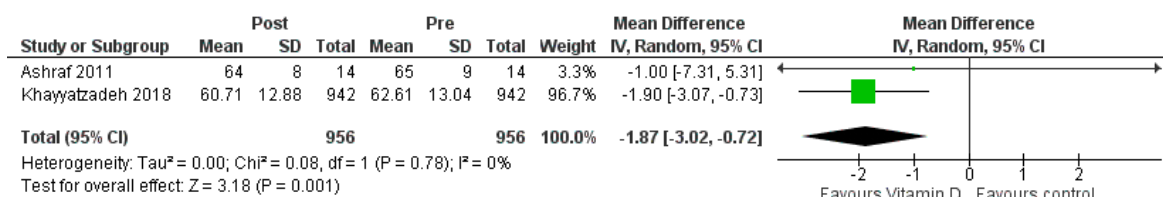
### **ClinicalTrial.gov**

Hypertension | Vitamin D | Child  
Applied filter: Child (birth-17)

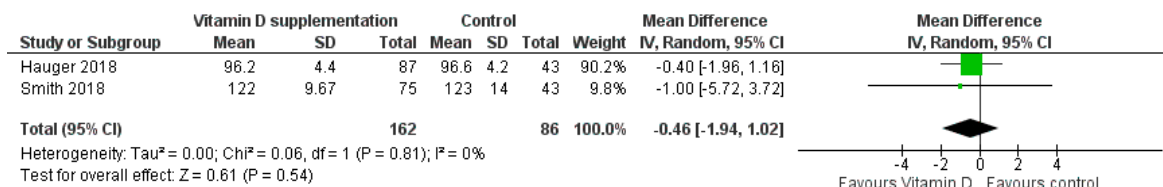
### **Supplement Figure S1: Sensitivity analyses**



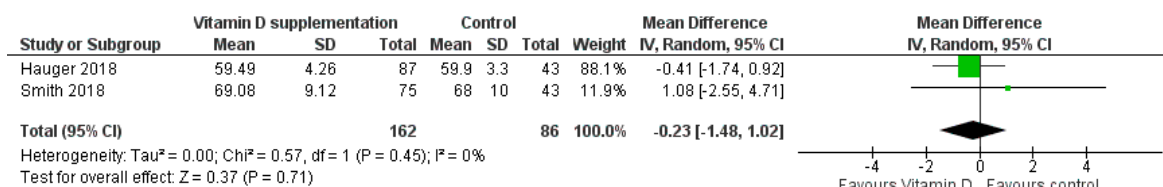
**Figure a.** Forest plot of sensitivity analysis of mean differences in SBP (in mmHg) before and after subjects receiving vitamin D supplementation (excluding vitamin D sufficient patients from Khayatzadeh, 2018).



**Figure b.** Forest plot of sensitivity analysis of mean differences in DBP (in mmHg) before and after subjects receiving vitamin D supplementation (excluding vitamin D sufficient patients from Khayatzadeh, 2018).



**Figure c.** Forest plot of sensitivity analysis of mean differences in SBP (in mmHg) between subjects receiving vitamin D supplementation compared with their comparators (excluding Al Daghri, 2019 as the source of heterogeneity).



**Figure d.** Forest plot of sensitivity analysis of mean differences in SBP (in mmHg) between subjects receiving vitamin D supplementation compared with their comparators (excluding Al Daghri, 2019 which included only vitamin D deficient patients)

**Figure S1.** Meta-analysis of the sensitivity analyses of the effects of vitamin D supplementation on SBP and DBP. Mean differences for each study are represented by squares, and 95% CIs are represented by the lines through the squares. The pooled mean differences are represented by diamonds. Between-study heterogeneity was assessed with the use of the I<sup>2</sup> statistic. SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

**Supplement: GRADEing of the Meta-analysis**

**Table S1: Quality of evidence of NRS and RCTs**

NRS	Certainty assessment					No of patients		Effect	Certainty
	No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Pre-supplementation	Post-supplementation	
<b>Systolic blood pressure</b>									
2	Observational studies	Not serious	Not serious	Not serious	Serious <sup>b</sup>	1002	1002	MD 0.33 higher (0.93 lower to 1.58 higher)	⊕○○○ VERY LOW
<b>Diastolic blood pressure</b>									
2	Observational studies	Not serious	Not serious	Not serious	Not serious	1002	1002	MD 2.26 lower (3.4 lower to 1.12 lower)	⊕⊕○○ LOW
RCTs	Certainty assessment					No of patients		Effect	Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Supplementation	No supplementation	Absolute (95% CI)	
<b>Systolic blood pressure</b>									
3	Randomized trials	Not serious <sup>a</sup>	Serious <sup>c</sup>	Not serious	Serious <sup>b</sup>	328	266	MD 2.04 lower (5.12 lower to 1.04 higher)	⊕⊕○○ LOW
<b>Diastolic blood pressure</b>									
3	Randomized trials	Not serious <sup>a</sup>	Not serious	Not serious	Serious <sup>b</sup>	328	266	MD 0.01 higher (1.09 lower to 1.12 higher)	⊕⊕⊕○ MODERATE

CI: Confidence interval; MD: Mean difference; NRS: Non-randomized human interventions study; RCT: Randomized controlled trial

**Explanations**

- a. Al Daghri (2019) has some risk of bias with respect to blinding of participants, personnel and outcome assessors and to other bias. It contributed to only 21% of the weight.
- b. Downgraded by one level due to serious imprecision. Confidence interval crosses the line of no effect.
- c. Downgraded by one level due to serious inconsistency. Unexplained heterogeneity I<sup>2</sup>=71%.



**Table S2: Sensitivity analyses of the quality of evidence of NRS and RCTs**

NRS	Certainty assessment					No of patients		Effect	Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Vitamin D supplementation	No supplementation	Absolute (95% CI)	
<b>Systolic blood pressure (excluding vitamin D sufficient patients from Khayyat-zadeh, 2018)</b>									
2	Observational studies	Not serious	Not serious	Not serious	Serious <sup>a</sup>	956	956	MD 0.39 higher (0.9 lower to 1.68 higher)	⊕○○○ VERY LOW
<b>Diastolic blood pressure (excluding vitamin D sufficient patients from Khayyat-zadeh, 2018)</b>									
2	Observational studies	Not serious	Not serious	Not serious	Not serious	956	956	MD 1.87 lower (3.02 lower to 0.72 lower)	⊕⊕○○ LOW
RCTs	Certainty assessment					No of patients		Effect	Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Vitamin D supplementation	No supplementation	Absolute (95% CI)	
<b>Systolic blood pressure (excluding Al Dag-hri, 2019 as the source of heterogeneity)</b>									
2	Randomized trials	Not serious	Not serious	Not serious	Serious <sup>a</sup>	162	86	MD 0.46 lower (1.94 lower to 1.02 higher)	⊕⊕⊕○ MODERATE
<b>Diastolic blood pressure (excluding Al Dag-hri, 2019 which included only vitamin D deficient patients)</b>									
2	Randomized trials	Not serious	Not serious	Not serious	Serious <sup>a</sup>	162	86	MD 0.23 lower (1.48 lower to 1.02 higher)	⊕⊕⊕○ MODERATE

CI: Confidence interval; MD: Mean difference; NRS: Non-randomized human interventions study; RCT: Randomized controlled trial

**Explanations**

a. Downgraded by one level due to serious imprecision. Confidence interval crosses the line of no effect.