Supplementary material 1 (Supplementary methodology)

Definition of bronchiolitis

Bronchiolitis was diagnosed according to the Clinical Practice Guidelines of the American Academy of Pediatrics [1] as a constellation of symptoms and clinical signs occurring in children below two years of age that includes increasing respiratory efforts and wheezing preceded by a viral upper respiratory tract prodrome with the exclusion of other causes of wheezy chest. Common clinical manifestations are rhinorrhea, cough, tachypnea, wheezing, crepitations, and increased work of breathing, including chest retractions, grunting, and nasal flaring. Radiographic and laboratory studies are not routinely performed unless in the case of suspected other diagnosis (e.g., bacterial infection) or complication (e.g., pneumothorax). The term is generally applied for the first wheezing episode.

Wang Respiratory Score

This relies on clinical observation of four parameters (general appearance, respiratory rate, wheezing, and retractions). The score ranges from 0 to 12, where children with a score ≤ 3 can be treated on an outpatient basis, those with scores 4-8 commonly require hospital admission, and those with scores > 8 usually require PICU admission [2].

Parameters	**Score**			
	0	**1**	**2**	**3**
Respiratory rate (breath/min)	<30	31-45	46-60	>60
Wheezing	None	Terminal expiration or only with stethoscope	Entire expiration or audible on expiration without stethoscope	Inspiration and expiration without stethoscope
Retractions	None	Intercostal only	Tracheosternal	Severe with nasal flaring
General condition	Normal			Irritable, lethargic, poor feeding

Feeding Adequacy Scale

This is based on 10 points visual analog scale, on which parents rate feeding (including appetite, amount of food/drink, time spent feeding, and difficulty feeding) of their child from 0 (no feeding at all) to 10 (feeding as during healthy status) [3].

Assessment of serum 25 hydroxyvitamin D [25(OH)D) and ionized calcium levels

Serum levels of 25(OH)D and ionized calcium were measured at baseline and after 3 days, as previously described [4,5]. In brief, 3-ml blood samples were obtained from peripheral veins, centrifuged at 3000 rpm for 5 min, and the sera were stored at -80 till analysis. Total serum 25(OH)D levels were measured by chemiluminescence microparticle immunoassay method using ARCHITECT i2000SR immunoassay analyzer (Abbot Diagnostics, Lake Forest, IL, USA) and ARCHITECT 25-OH Vitamin D Reagent Kits (Abbot Diagnostics), according to manufacturer's directions. The assay range was from 8.0 ng/mL to 160 ng/ml. Serum ionized calcium was measured by Roche/Hitachi Cobas c analyzer (Roche Diagnostics, Santa Clara, California, USA) using the kit supplied by Roche, following manufacturer guidelines.

Criteria of hospital discharge for children with acute bronchiolitis

- No fever (body temperature <38°C)
- Oxygen saturation > 92% on room air
- Normal respiratory rate for age, using the World Health Organization age-specific criteria (<50 breaths/min for 2-12 months, <40 breaths/min for 1 to 5 years)
- Adequate feeding (defined as a Feeding Adequacy Scale of ≥ 7)
- Proper parent education and social support: to call their primary care provider or return to the emergency ward when the following manifestations of worsening clinical condition are observed:

- Increasing respiratory rate and/or work of breathing as indicated by accessory muscle use (e.g., breathing very fast and/or skin sucking in around the neck or ribs with each breath).
- Inability to maintain adequate hydration (e.g., unable to feed or drink by mouth or has not had a wet diaper in more than 6 to 8 hours).
- Worsening general appearance (has new symptoms not present while in the hospital such as vomiting or fever, looks lethargic or does not respond normally to touch or sound, change in baby's color)

References

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3. Sebastian A, Borkhoff CM, Wahi G, Giglia L, Bayliss A, Kanani R, et al. A Feeding Adequacy Scale for Children With Bronchiolitis: Prospective Multicenter Study. Hosp Pediatr. 2023;13: 895–903. doi:10.1542/hpeds.2023-007339
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5. Hussein MT, Yousef LM, Abdelwahed SA. Serum levels of vitamin D, magnesium, and calcium in patients with stable bronchial asthma. Egypt J Chest Dis Tuberc. 2019;68: 542–545. doi:10.4103/ejcdt.ejcdt_204_18

Supplementary material 2

Baseline characteristics of study participants in the whole cohort stratified by vitamin D status

Characteristics	**Total** (*n*=146)	**Serum 25(OH)D <30 ng/ml** (*n*=73)	**Serum 25(OH)D ≥30 ng/ml** (*n*=73)	***P* value**
Age (mon)*	6 (4-9)	5 (3-8)	6 (4-9)	0.180
Male sex#	97 (66.4%)	45 (61.6%)	52 (71.2%)	0.220
Body mass index (kg/m^2)$	17.2 (2.85)	17.3 (3.12)	17.09 (2.55)	0.591
Breastfeeding#	103 (70.6%)	50 (68.5%)	53 (72.6%)	0.586
Parental smoking#	85 (58.2%)	41 (56.2%)	44 (60.3%)	0.615
Family history of allergy#	27 (18.5%)	16 (21.9%)	11 (15.1%)	0.286
Allergies#	10 (6.9%)	9 (12.3%)	1 (1.4%)	0.017[a]
Regular vitamin D intake#	94 (64.4%)	46 (63.0%)	48 (65.8%)	0.730
Time from disease onset to admission (h)*	45.5 (24-72)	45 (24-72)	47 (26-70)	0.660
Time from admission to randomization (h)*	8 (4-12)	7 (4-12)	9 (5-12)	0.632
Respiratory rate (breath/min)$	53.9 (6.37)	55.2 (6.7)	52.5 (5.8)	0.010[a]
Oxygen saturation (%)$	89.2 (0.94)	89.3 (0.91)	89.1 (0.94)	0.194
Wang respiratory score$	8.5 (1.01)	8.6 (1.06)	8.4 (0.95)	0.325
Feeding adequacy scale$	5.8 (1.12)	5.9 (1.14)	5.7 (1.10)	0.212
Oxygen supplementation (L/min)$	1.8 (0.45)	1.7 (0.46)	1.8 (0.44)	0.269
Parenteral fluids#	150 (100%)	73 (100%)	73 (100%)	1.000
Tube feeding#	82 (56.2%)	38 (52.1%)	44 (60.3%)	0.317
Serum ionized calcium (mmol/L)$	1.15 (0.12)	1.17 (0.13)	1.14 (0.10)	0.154
Randomized to intervention arm	73 (50%)	35 (48.0%)	38 (52.1%)	0.619

*median (IQR), #number (%), $mean (SD)

[a]*P* <0.05

25(OH)D, 25-hydroxyvitamin D

Supplementary material 3

Baseline characteristics between randomized study groups within the subgroup of participants with baseline serum 25-hydroxyvitamin D levels <30 ng/mL (pre-specified vitamin D deficiency/insufficiency subgroup, *n*=73)

Characteristics	**Study group** (*n*=35)	**Comparison group** (*n*=38)	***p*-value**
Age (mon)*	5 (4-9)	5.5 (3-8)	0.867
Male sex#	22 (62.9%)	23 (60.5%)	0.838
Body mass index (kg/m^2)$	16.9 (2.99)	17.8 (3.23)	0.248
Breastfeeding#	22 (62.9%)	28 (73.7%)	0.320
Parental smoking#	21 (60.0%)	20 (52.6%)	0.526
Family history of allergy#	10 (28.6%)	16 (15.8%)	0.187
Allergies#	5 (14.3%)	4 (10.5%)	0.729
Regular vitamin D intake#	21 (60.0%)	25 (65.8%)	0.609
Time from disease onset to admission (h)*	45 (24-72)	45 (24-72)	0.969
Time from admission to randomization (h)*	8 (4-12)	7 (4-13)	0.642
Respiratory rate (breath/min)$	54.4 (5.30)	56 (7.68)	0.308
Oxygen saturation (%)$	89.5 (0.85)	89.2 (0.96)	0.252
Wang respiratory score$	8.4 (0.97)	8.7 (1.11)	0.172
Feeding adequacy scale$	5.9 (1.37)	6.0 (0.90)	0.819
Oxygen supplementation (L/min)$	1.6 (0.49)	1.8 (0.41)	0.133
Parenteral fluids#	35 (100%)	38 (100%)	1.000
Tube feeding#	18 (51.4%)	20 (52.6%)	0.918
Serum ionized calcium (mmol/L)$	1.178 (0.12)	1.16 (0.14)	0.830
Serum 25-hydroxyvitamin D (ng/mL)$	19.5 (6.6)	18.2 (6.0)	0.386

*median (IQR), #number (%), $mean (SD)

Supplementary material 4

Results of linear regression models for the homogeneity of the intervention (vitamin D supplementation) effect on primary outcome over selected factors

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Codes key:
bmi:body mass index
farcolin2: nebulized beta-2 agonists therapy
feedscore: Feeding Adequacy Scale
ohd1: baseline serum 25 hydroxyvitamin D
spo2: oxygen saturation
steroid2: systemic corticosteroids therapy
tdis: time from randomization to discharge
vitd: bolus vitamin D3 supplementation (intervention)
wang: Wang Respiratory Score

. regress tdis i.vitd c.ohd1 i.vitd#c.ohd1

      Source |       SS           df       MS      Number of obs   =       146
-------------+----------------------------------   F(3, 142)       =      4.49
       Model |  27489.7912         3  9163.26375   Prob > F        =    0.0048
    Residual |  289477.448       142  2038.57358   R-squared       =    0.0867
-------------+----------------------------------   Adj R-squared   =    0.0674
       Total |   316967.24       145  2185.98096   Root MSE        =    45.151

------------------------------------------------------------------------------
        tdis | Coefficient  Std. err.      t    P>|t|     [95% conf. interval]
-------------+----------------------------------------------------------------
      1.vitd |  -66.89921   18.81732    -3.56   0.001    -104.0975   -29.70094
        ohd1 |   -.644607   .3961364    -1.63   0.106    -1.427694    .1384798
             |
 vitd#c.ohd1 |
          1  |   1.666409   .5657118     2.95   0.004     .5481034    2.784714
             |
       _cons |   170.1462   12.85994    13.23   0.000     144.7245    195.5679
------------------------------------------------------------------------------

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```
. regress tdis i.vitd c.age i.vitd#c.age

      Source |       SS           df       MS      Number of obs   =       146
-------------+----------------------------------   F(3, 142)       =      1.80
       Model |  11634.0024         3  3878.00079   Prob > F        =    0.1493
    Residual |  305333.237       142  2150.23407   R-squared       =    0.0367
-------------+----------------------------------   Adj R-squared   =    0.0164
       Total |   316967.24       145  2185.98096   Root MSE        =    46.371

------------------------------------------------------------------------------
        tdis | Coefficient  Std. err.      t    P>|t|     [95% conf. interval]
-------------+----------------------------------------------------------------
      1.vitd |  -26.23329   14.61351    -1.80   0.075    -55.12145     2.65486
         age |  -1.355288   1.244155    -1.09   0.278    -3.814748    1.104172
             |
  vitd#c.age |
          1  |    1.53363   1.804846     0.85   0.397    -2.034209    5.101469
             |
       _cons |   160.3234   10.08157    15.90   0.000     140.3941    180.2528
------------------------------------------------------------------------------

.
. regress tdis i.vitd i.male i.vitd#i.male

      Source |       SS           df       MS      Number of obs   =       146
-------------+----------------------------------   F(3, 142)       =      1.77
       Model |  11428.1228         3  3809.37426   Prob > F        =    0.1555
    Residual |  305539.117       142  2151.68392   R-squared       =    0.0361
-------------+----------------------------------   Adj R-squared   =    0.0157
       Total |   316967.24       145  2185.98096   Root MSE        =    46.386

------------------------------------------------------------------------------
        tdis | Coefficient  Std. err.      t    P>|t|     [95% conf. interval]
-------------+----------------------------------------------------------------
      1.vitd |  -26.70234   13.27812    -2.01   0.046    -52.95068   -.4540017
      1.male |  -10.16858   11.33744    -0.90   0.371    -32.58056     12.2434
             |
   vitd#male |
        1 1  |   16.61553   16.28259     1.02   0.309    -15.57207    48.80314
             |
       _cons |   157.6154   9.097092    17.33   0.000     139.6322    175.5986
------------------------------------------------------------------------------
```

```
.
. regress tdis i.vitd c.bmi i.vitd#c.bmi

      Source |       SS           df       MS      Number of obs   =       146
-------------+----------------------------------   F(3, 142)       =      2.33
       Model |  14891.6962         3  4963.89874   Prob > F        =    0.0766
    Residual |  302075.543       142  2127.29256   R-squared       =    0.0470
-------------+----------------------------------   Adj R-squared   =    0.0268
       Total |   316967.24       145  2185.98096   Root MSE        =    46.123

------------------------------------------------------------------------------
        tdis | Coefficient  Std. err.      t    P>|t|     [95% conf. interval]
-------------+----------------------------------------------------------------
      1.vitd |   17.69545   47.26813     0.37   0.709    -75.74471    111.1356
         bmi |    2.87778   1.813418     1.59   0.115    -.7070058    6.462565
             |
  vitd#c.bmi |
          1  |  -1.907883    2.71229    -0.70   0.483    -7.269567    3.453802
             |
       _cons |   101.0866   31.95508     3.16   0.002     37.91748    164.2558
------------------------------------------------------------------------------

.
. regress tdis i.vitd i.steroid2 i.vitd#i.steroid2

      Source |       SS           df       MS      Number of obs   =       146
-------------+----------------------------------   F(3, 142)       =      6.49
       Model |  38214.0409         3  12738.0136   Prob > F        =    0.0004
    Residual |  278753.199       142   1963.0507   R-squared       =    0.1206
-------------+----------------------------------   Adj R-squared   =    0.1020
       Total |   316967.24       145  2185.98096   Root MSE        =    44.306

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> -
         tdis | Coefficient  Std. err.      t    P>|t|     [95% conf. interval
> ]
--------------+---------------------------------------------------------------
> -
       1.vitd |  -23.05172   8.227479    -2.80   0.006    -39.31589   -6.78755
> 4
   1.steroid2 |  -47.91379   12.83416    -3.73   0.000    -73.28451   -22.5430
> 8
              |
vitd#steroid2 |
         1 1  |   35.58506   18.15025     1.96   0.052    -.294552    71.4646
> 7
```

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             |
       _cons |   160.9138   5.817706    27.66   0.000     149.4133    172.414
> 3
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> -

.
. regress tdis i.vitd i.farcolin2 i.vitd#i.farcolin2

      Source |       SS           df       MS      Number of obs   =       146
-------------+----------------------------------   F(3, 142)       =      4.01
       Model |  24737.9525         3  8245.98417   Prob > F        =    0.0090
    Residual |  292229.287       142  2057.95273   R-squared       =    0.0780
-------------+----------------------------------   Adj R-squared   =    0.0586
       Total |   316967.24       145  2185.98096   Root MSE        =    45.365

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> --
         tdis | Coefficient  Std. err.      t    P>|t|     [95% conf. interva
> l]
--------------+---------------------------------------------------------------
> --
       1.vitd |       1.95   30.43154     0.06   0.949    -58.20741    62.107
> 41
  1.farcolin2 |   50.74412   21.02034     2.41   0.017     9.190885    92.297
> 35
              |
vitd#farcolin2 |
         1 1  |  -19.45064   31.40331    -0.62   0.537    -81.52906    42.627
> 78
              |
        _cons |      103.8   20.28769     5.12   0.000     63.69506    143.90
> 49
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> --
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```
.
. regress tdis i.vitd c.spo2 i.vitd#c.spo2

      Source |       SS           df       MS      Number of obs   =       146
-------------+----------------------------------   F(3, 142)       =      4.05
       Model |  24970.8407         3  8323.61357   Prob > F        =    0.0085
    Residual |  291996.399       142  2056.31267   R-squared       =    0.0788
-------------+----------------------------------   Adj R-squared   =    0.0593
       Total |   316967.24       145  2185.98096   Root MSE        =    45.347

------------------------------------------------------------------------------
        tdis | Coefficient  Std. err.      t    P>|t|     [95% conf. interval]
-------------+----------------------------------------------------------------
      1.vitd |  -6.803329   719.0024    -0.01   0.992    -1428.135    1414.529
        spo2 |  -11.16813   5.609793    -1.99   0.048    -22.25763   -.0786342
             |
 vitd#c.spo2 |
          1  |  -.0950472   8.062667    -0.01   0.991    -16.03342    15.84332
             |
       _cons |   1146.715    500.145     2.29   0.023     158.0231    2135.407
------------------------------------------------------------------------------

.
. regress tdis i.vitd c.wang i.vitd#c.wang

      Source |       SS           df       MS      Number of obs   =       146
-------------+----------------------------------   F(3, 142)       =      7.10
       Model |  41368.0913         3  13789.3638   Prob > F        =    0.0002
    Residual |  275599.148       142  1940.83907   R-squared       =    0.1305
-------------+----------------------------------   Adj R-squared   =    0.1121
       Total |   316967.24       145  2185.98096   Root MSE        =    44.055

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        tdis | Coefficient  Std. err.      t    P>|t|     [95% conf. interval]
-------------+----------------------------------------------------------------
      1.vitd |   147.1085   64.41851     2.28   0.024     19.76524    274.4517
        wang |   18.77301   4.601275     4.08   0.000     9.677161    27.86886
             |
 vitd#c.wang |
          1  |  -19.35386   7.547709    -2.56   0.011    -34.27426   -4.433468
             |
       _cons |  -6.830544   39.04312    -0.17   0.861    -84.01141    70.35032
------------------------------------------------------------------------------
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```
.
. regress tdis i.vitd c.feedscore i.vitd#c.feedscore

      Source |       SS           df       MS      Number of obs   =       146
-------------+----------------------------------   F(3, 142)       =      7.16
       Model |  41668.9166         3  13889.6389   Prob > F        =    0.0002
    Residual |  275298.323       142  1938.72059   R-squared       =    0.1315
-------------+----------------------------------   Adj R-squared   =    0.1131
       Total |   316967.24       145  2185.98096   Root MSE        =    44.031

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> ----
            tdis | Coefficient  Std. err.      t    P>|t|     [95% conf. inter
> val]
-----------------+------------------------------------------------------------
> ----
          1.vitd |  -43.79119   39.80153    -1.10   0.273    -122.4713    34.8
> 8891
       feedscore |  -16.01796   5.314962    -3.01   0.003    -26.52464   -5.51
> 1288
                 |
vitd#c.feedscore |
              1  |   4.543186   6.726587     0.68   0.501    -8.754005    17.8
> 4038
                 |
           _cons |    244.982   31.58495     7.76   0.000     182.5446    307.
> 4195
------------------------------------------------------------------------------
> ----

.
. capture log close
```