

Supplementary Figure

CSF 25(OH)D₃

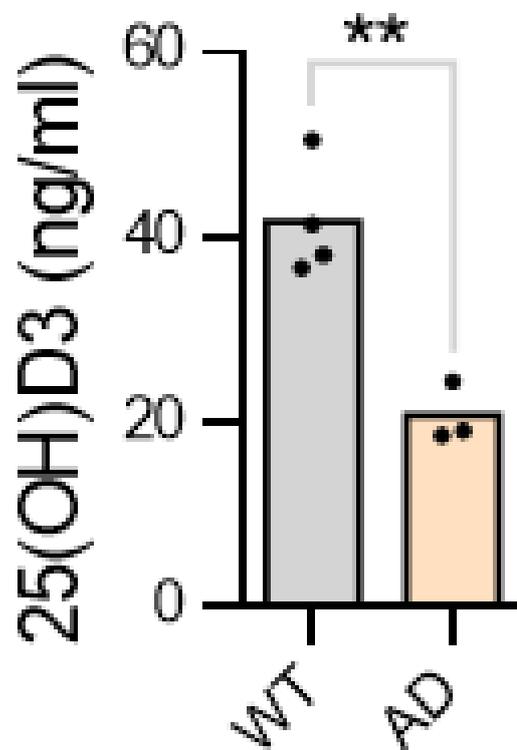


Figure S1. Cerebrospinal fluid (CSF) 25(OH)D₃ levels in APP/PS1 mice. 25(OH)D₃ levels in serum and CSF were determined by Vitamin D₃ EIA Kit and the results are shown as mean \pm SEM. *P<0.05 by unpaired t-test.

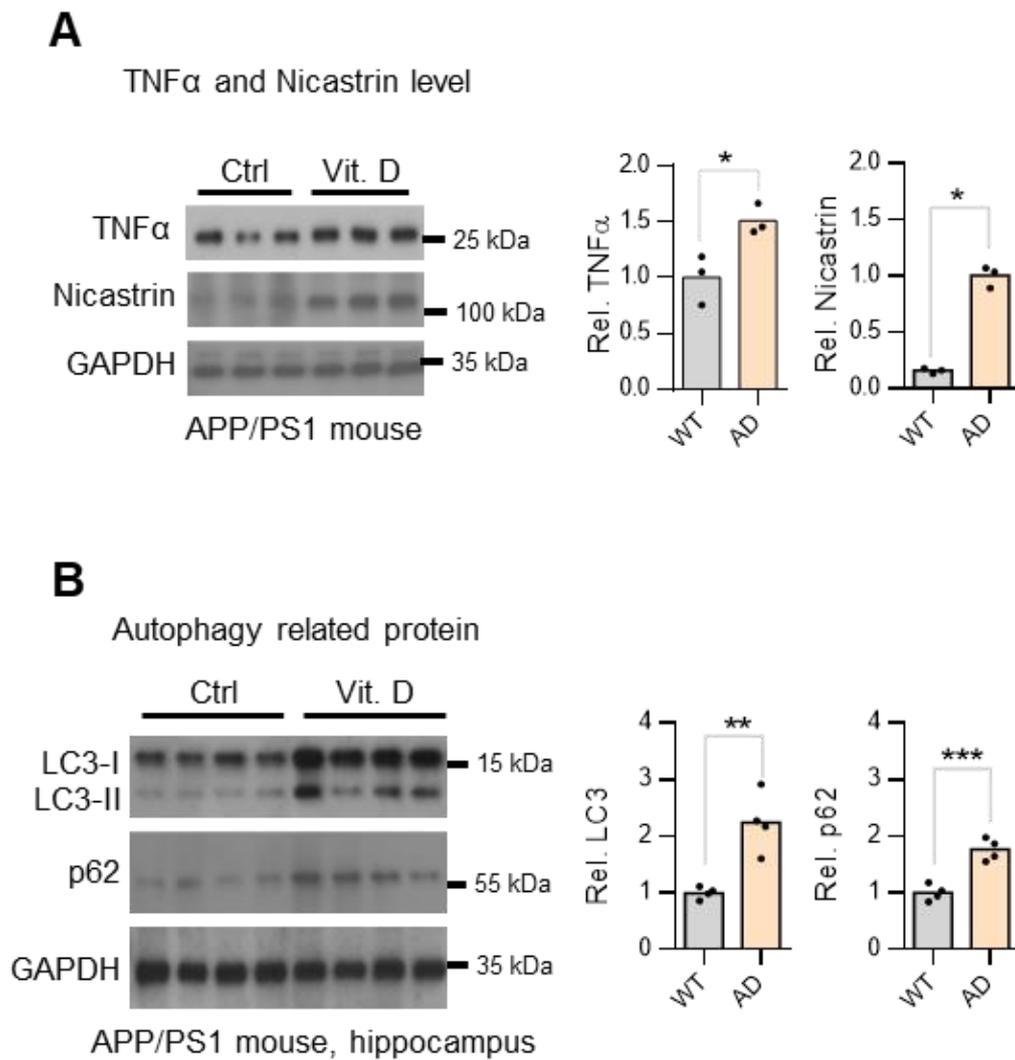


Figure S2. Western blot analysis of inflammatory cytokine and APP processing-related proteins in the hippocampus of APP/PS1 mice supplemented with or without cholecalciferol. (A) The western blots for hippocampal TNF α , Nicastrin and GAPDH. (B) The western blots for hippocampal LC3, p62 and GAPDH. Densitometrical quantification of target bands were normalized to GAPDH. *P<0.05; **P<0.01; ***P < 0.05 by unpaired t-test (right panel).

Serum 25(OH)D₃

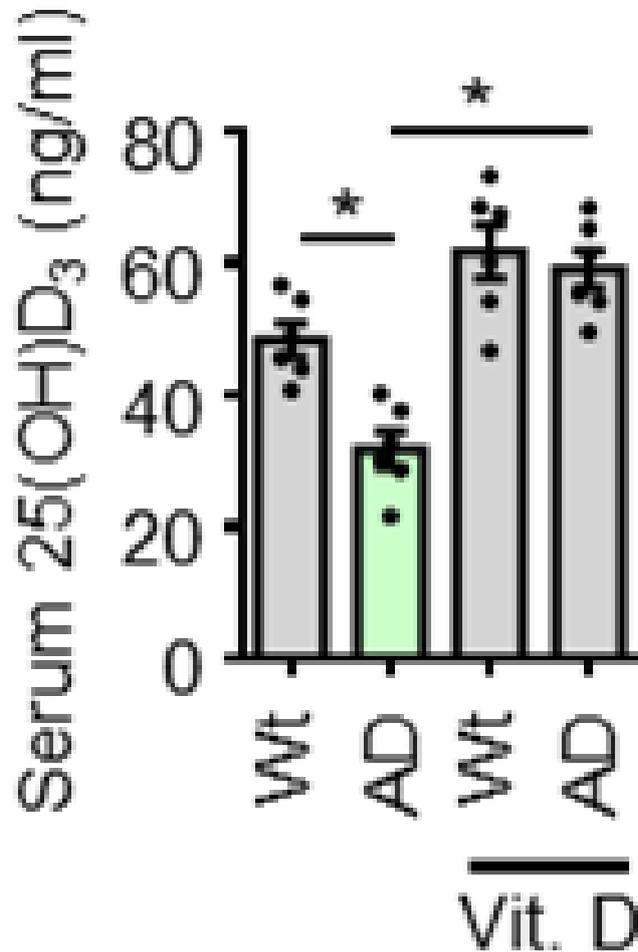


Figure S3. Cholecalciferol supplementation restores serum 25(OH)D₃ levels. 25(OH)D₃ levels in serum and CSF were determined by Vitamin D3 EIA Kit and the results are shown as mean \pm SEM. *P<0.05 by unpaired t-test.

Table S1. Calcitriol use in people aged over 65 years is associated with increased risk of dementia.

Dosage (mcg/year) [#]	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
2.5-10.95	1.04 (0.91-1.19)	0.5535	1.04 (0.91-1.19)	0.5833
10.95-36.5	1.26 (1.09-1.46)	0.0021*	1.27 (1.09-1.47)	0.0016*
>36.5	1.83 (1.57-2.13)	<.0001*	1.80 (1.54-2.09)	<.0001*

Dosage (mcg/year) is the assumed average maintenance dose per year for a calcitriol used in the whole follow-up.

*Significantly different from control group at P < 0.05.

Table S2. Over-supplementation of calcitriol in males aged over 65 years is linked to an increased incidence of dementia (n=5362).

Dosage (mcg/year) [#]	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
2.5-10.95	1.12 (0.89-1.42)	0.3423	1.12 (0.89-1.42)	0.3314
10.95-36.5	1.14 (0.88-1.48)	0.3243	1.14 (0.88-1.49)	0.3201
>36.5	1.85 (1.44-2.39)	<.0001	1.81 (1.40-2.34)	<.0001*

Dosage (mcg/year) is the assumed average maintenance dose per year for a calcitriol used in the whole follow-up.

*Significantly different from control group at P < 0.05

Table S3. Over-supplementation of calcitriol in females aged over 65 years is linked to an increased incidence of dementia (n=9286).

Dosage (mcg/year) [#]	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
2.5-10.95	1.00 (0.85-1.18)	0.9864	1.00 (0.84-1.18)	0.9883
10.95-36.5	1.32 (1.11-1.58)	0.0020*	1.33 (1.12-1.59)	0.0015*
>36.5	1.82 (1.51-2.20)	<.0001*	1.78 (1.47-2.16)	<.0001*

Dosage (mcg/year) is the assumed average maintenance dose per year for a calcitriol used in the whole follow-up.

*Significantly different from control group at P < 0.05

Table S4. Over-supplementation of calcitriol in people aged 65-75 years is linked to an increased incidence of dementia (n=5196).

Dosage (mcg/year)[#]	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
2.5-10.95	0.95 (0.76-1.20)	0.6872	0.94 (0.75-1.19)	0.6114
10.95-36.5	1.40 (1.11-1.76)	0.0048*	1.41 (1.12-1.78)	0.0039*
>36.5	2.02 (1.56-2.61)	<.0001*	2.03 (1.57-2.63)	<.0001*

Dosage (mcg/year) is the assumed average maintenance dose per year for a calcitriol used in the whole follow-up.

*Significantly different from control group at P < 0.05

Table S5. Over-supplementation of calcitriol in people aged over 75 years is linked to an increased incidence of dementia (n=9452).

Dosage (mcg/year)[#]	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
2.5-10.95	1.10 (0.93-1.31)	0.2501	1.10 (0.93-1.31)	0.2496
10.95-36.5	1.21 (1.00-1.46)	0.0481	1.20 (0.99-1.45)	0.0571
>36.5	1.74 (1.44-2.09)	<.0001*	1.74 (1.45-2.10)	<.0001*

Dosage (mcg/year) is the assumed average maintenance dose per year for a calcitriol used in the whole follow-up.

*Significantly different from control group at P < 0.05

Table S6. Calcitriol use is associated with increased risk of mortality in dementia.

Dosage (mcg/year) [#]	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
<10.95	0.79 (0.53-1.18)	0.2483	0.83 (0.55-1.24)	0.3574
10.95-36.5	1.10 (0.73-1.66)	0.6370	1.17 (0.78-1.76)	0.4559
>36.5	2.39 (1.64-3.48)	<.0001*	2.17 (1.48-3.17)	<.0001*

[#] Dosage (mcg/year) is the assumed average maintenance dose per year for a calcitriol used in the whole follow-up.

*Significantly different from control group at P < 0.05.

Table S7. Over-supplementation of calcitriol is associated with decreased survival of male patients with pre-existing dementia. (n=315).

Dosage (mcg/year) [#]	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
<10.95	0.67 (0.34-1.33)	0.2533	0.65 (0.33-1.29)	0.2168
10.95-36.5	1.99 (1.12-3.54)	0.0195	1.97 (1.10-3.54)	0.0230
>36.5	1.89 (1.02-3.51)	0.0448	2.02 (1.06-3.84)	0.0330

[#] Dosage (mcg/year) is the assumed average maintenance dose per year for a calcitriol used in the whole follow-up.

*Significantly different from control group at P < 0.05.

Table S8. Over-supplementation of calcitriol is associated with decreased survival of female patients with pre-existing dementia. (n=665).

Dosage (mcg/year) [#]	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
<10.95	0.85 (0.52-1.40)	0.5180	0.94 (0.57-1.55)	0.8008
10.95-36.5	0.79 (0.44-1.41)	0.4213	0.85 (0.47-1.52)	0.5764
>36.5	2.67 (1.66-4.29)	<.0001*	2.50 (1.55-4.05)	0.0002*

[#] Dosage (mcg/year) is the assumed average maintenance dose per year for a calcitriol used in the whole follow-up.

*Significantly different from control group at P < 0.05.

Table S9. Over-supplementation of calcitriol is associated with decreased survival of 60-75 years-old patients with pre-existing dementia. (n=239).

Dosage (mcg/year) [#]	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
<10.95	1.47 (0.70-3.07)	0.3075	1.54 (0.72-3.27)	0.2657
10.95-36.5	1.30 (0.59-2.85)	0.5128	1.38 (0.59-3.21)	0.4587
>36.5	1.91 (0.69-5.26)	0.2134	1.35 (0.47-3.87)	0.5817

[#] Dosage (mcg/year) is the assumed average maintenance dose per year for a calcitriol used in the whole follow-up.

*Significantly different from control group at P < 0.05.

Table S10. Over-supplementation of calcitriol is associated with decreased survival of over 75 years-old patients with pre-existing dementia. (n=741).

Dosage (mcg/year) [#]	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
<10.95	0.63 (0.39-1.02)	0.0615	0.68 (0.42-1.10)	0.1169
10.95-36.5	1.05 (0.65-1.69)	0.8545	1.08 (0.67-1.74)	0.7669
>36.5	2.43 (1.62-3.65)	<.0001*	2.46 (1.63-3.71)	<.0001*

[#] Dosage (mcg/year) is the assumed average maintenance dose per year for a calcitriol used in the whole follow-up.

*Significantly different from control group at P < 0.05.