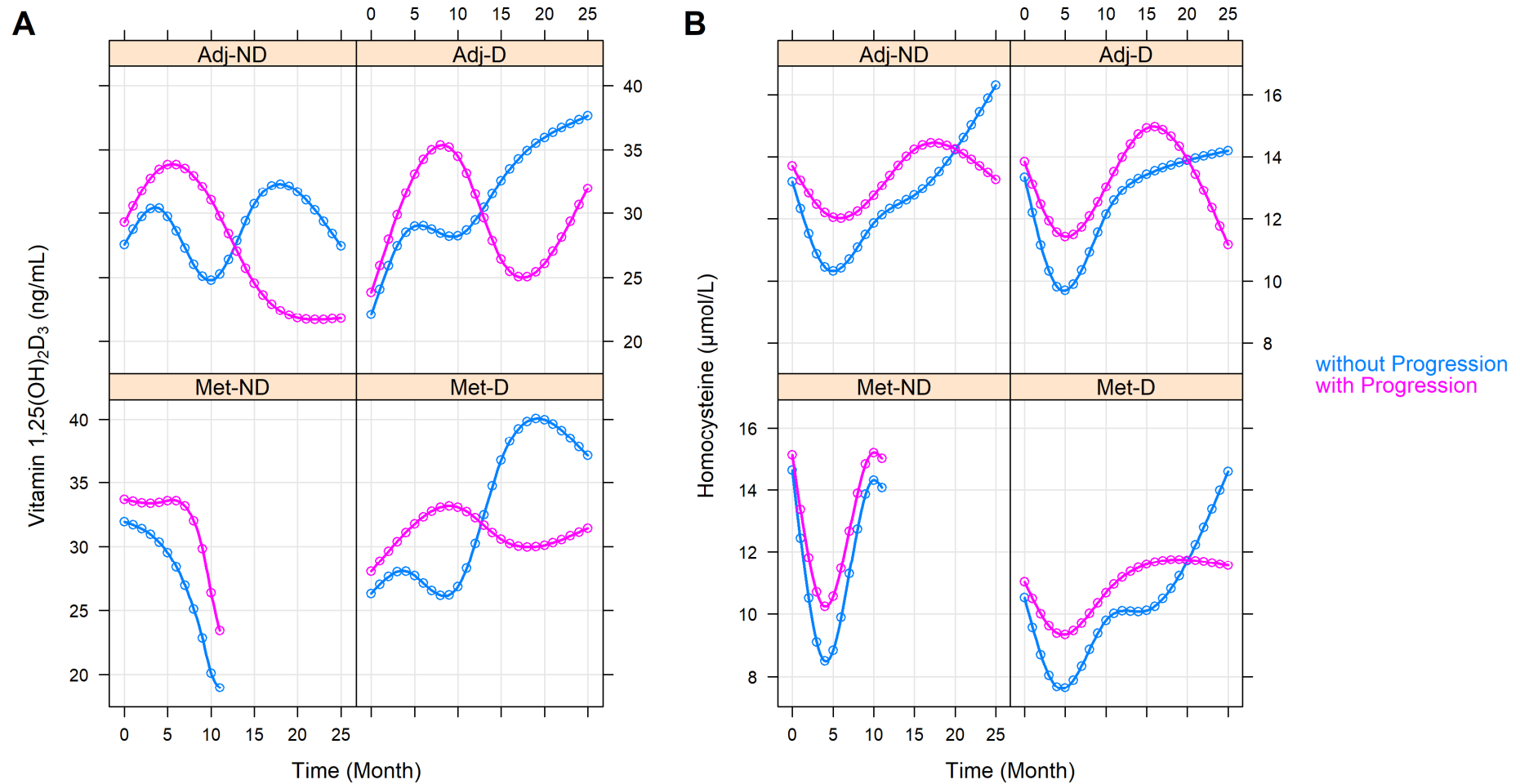
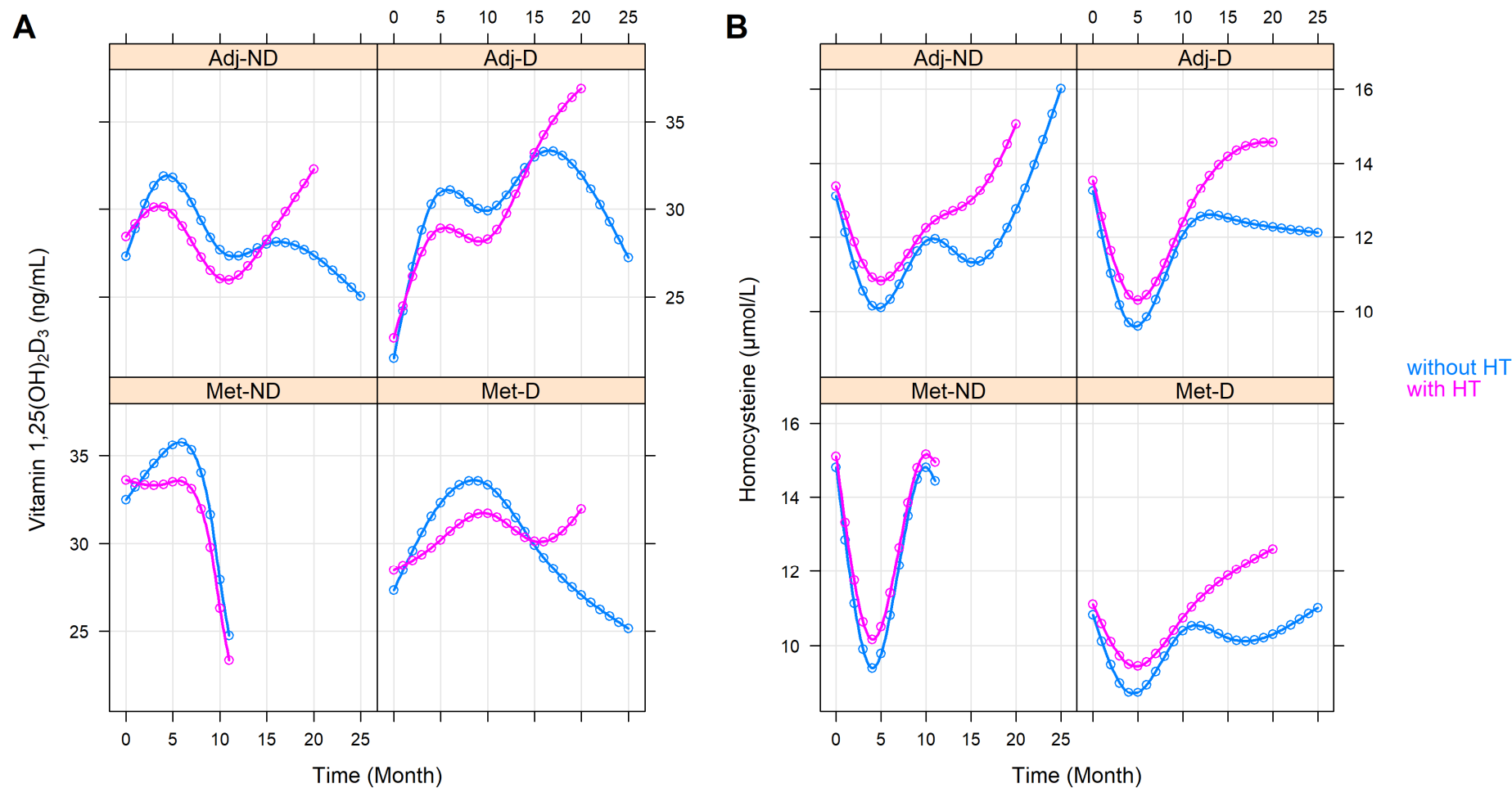


**Figure S1.** Predictions of average longitudinal changes in vitamin 1,25(OH)<sub>2</sub>D<sub>3</sub> (A) and homocysteine (B) level of the study groups throughout the first 25 months of the observation time, stratified by AJCC staging [22]. Adj-ND: patients without metastasis and no vitamin D<sub>3</sub> supplementation; Adj-D: patients without metastasis with vitamin D<sub>3</sub> supplementation; Met-ND: patients with metastasis and no vitamin D<sub>3</sub> supplementation; Met-D: patients with metastasis with vitamin D<sub>3</sub> supplementation.

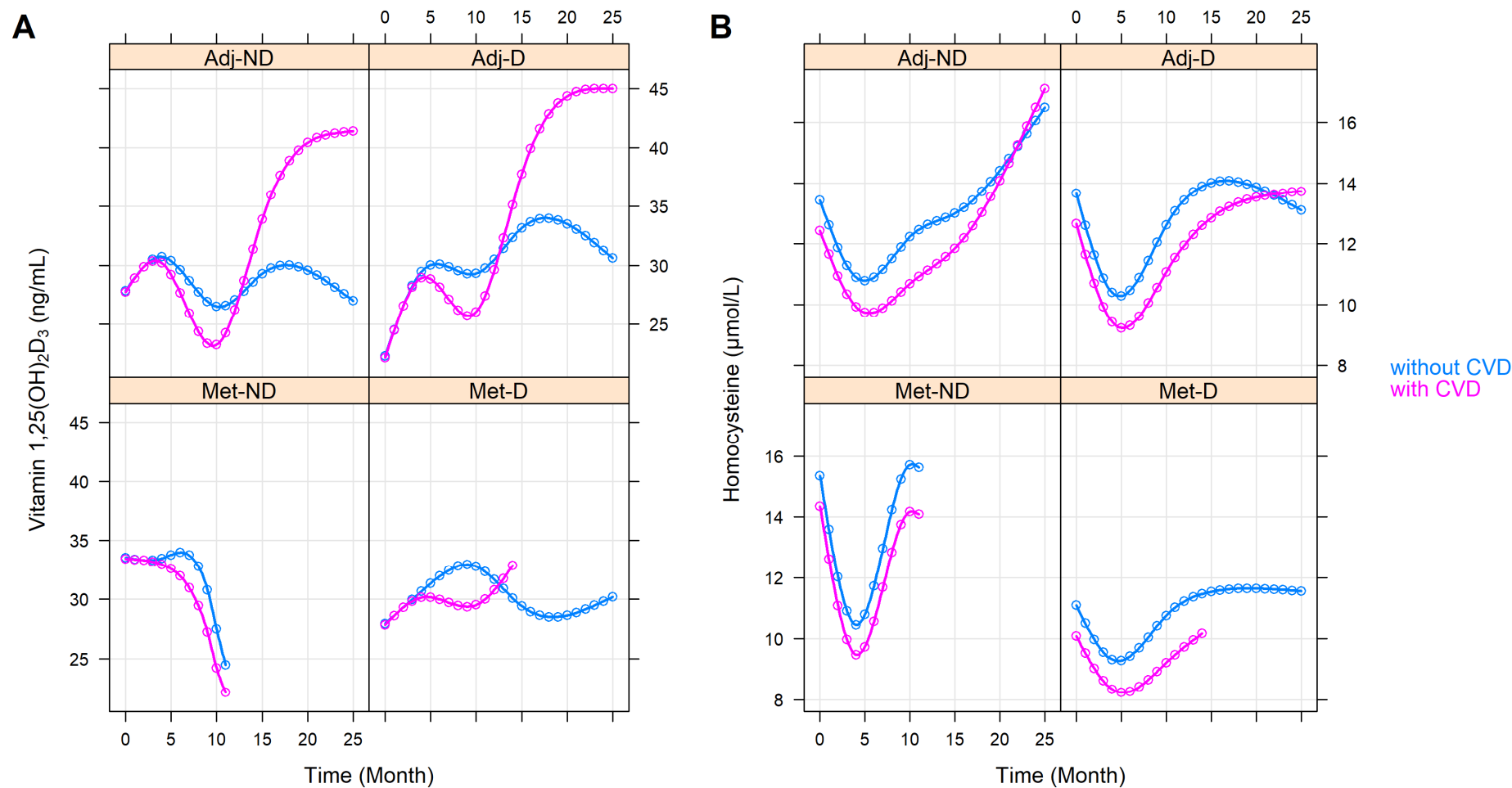
[22] Jessup, J.; Goldberg, R.; Asare, E.; Benson, A.; Brierley, J.; Chang, G.; Chen, V.; Compton, C.; De Nardi, P.; Goodman, K., et al. Colon and Rectum. In *AJCC Cancer Staging Manual (8th Edition)*, Amin, M., Edge, S., Greene, F., Byrd, D., Brookland, R., Washington, M., Gershengwald, J., Compton, C., Hess, K., Sullivan, D., et al., Eds. Springer International Publishing: Chicago, IL, USA, **2018**; pp. 251-274.



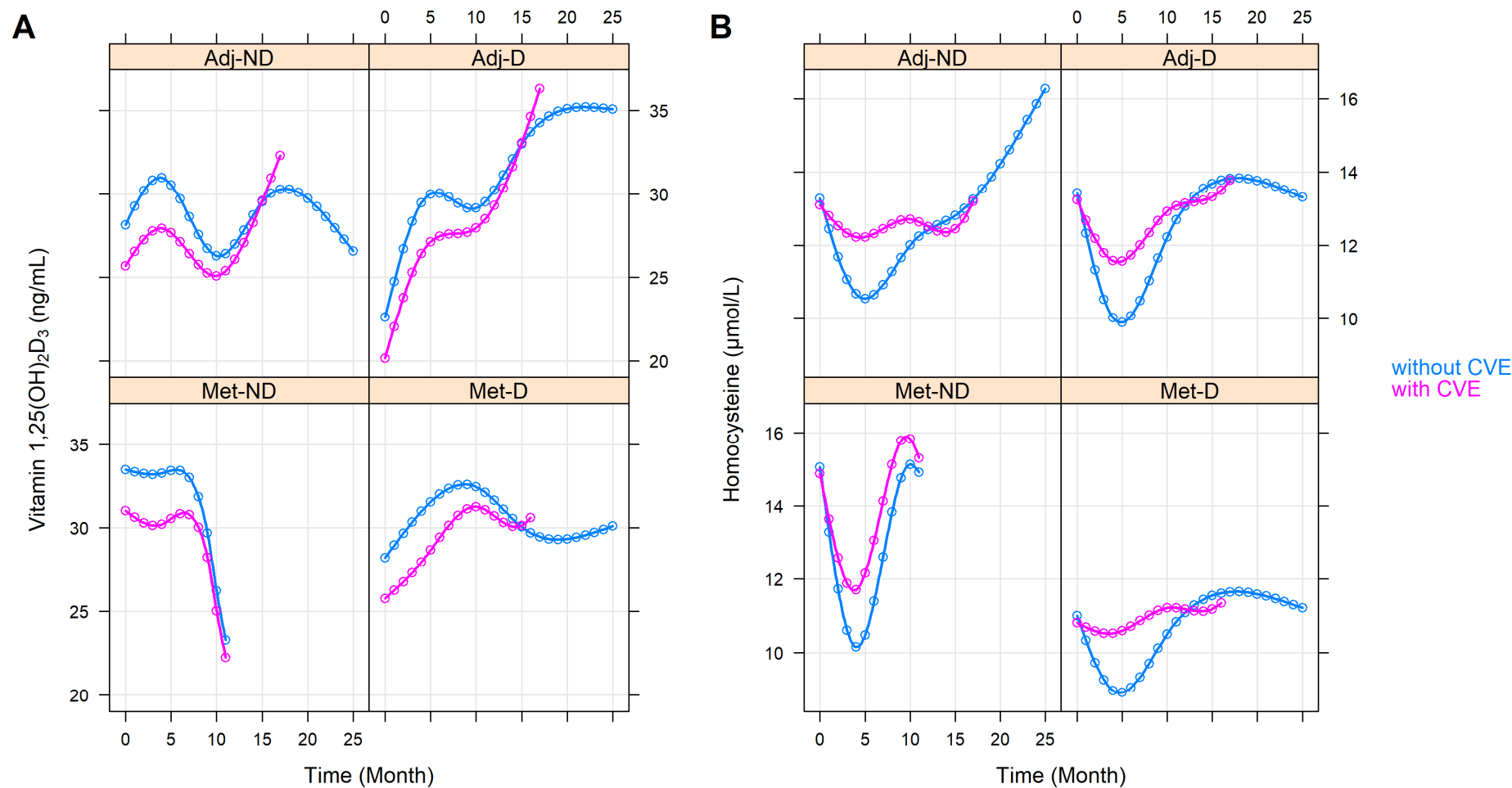
**Figure S2.** Predictions of average longitudinal changes in vitamin 1,25(OH)<sub>2</sub>D<sub>3</sub> (**A**) and homocysteine (**B**) level of the study groups throughout the first 25 months of the observation time, stratified by the occurrence of disease progression. Adj-ND: patients without metastasis and no vitamin D<sub>3</sub> supplementation; Adj-D: patients without metastasis with vitamin D<sub>3</sub> supplementation; Met-ND: patients with metastasis and no vitamin D<sub>3</sub> supplementation; Met-D: patients with metastasis with vitamin D<sub>3</sub> supplementation.



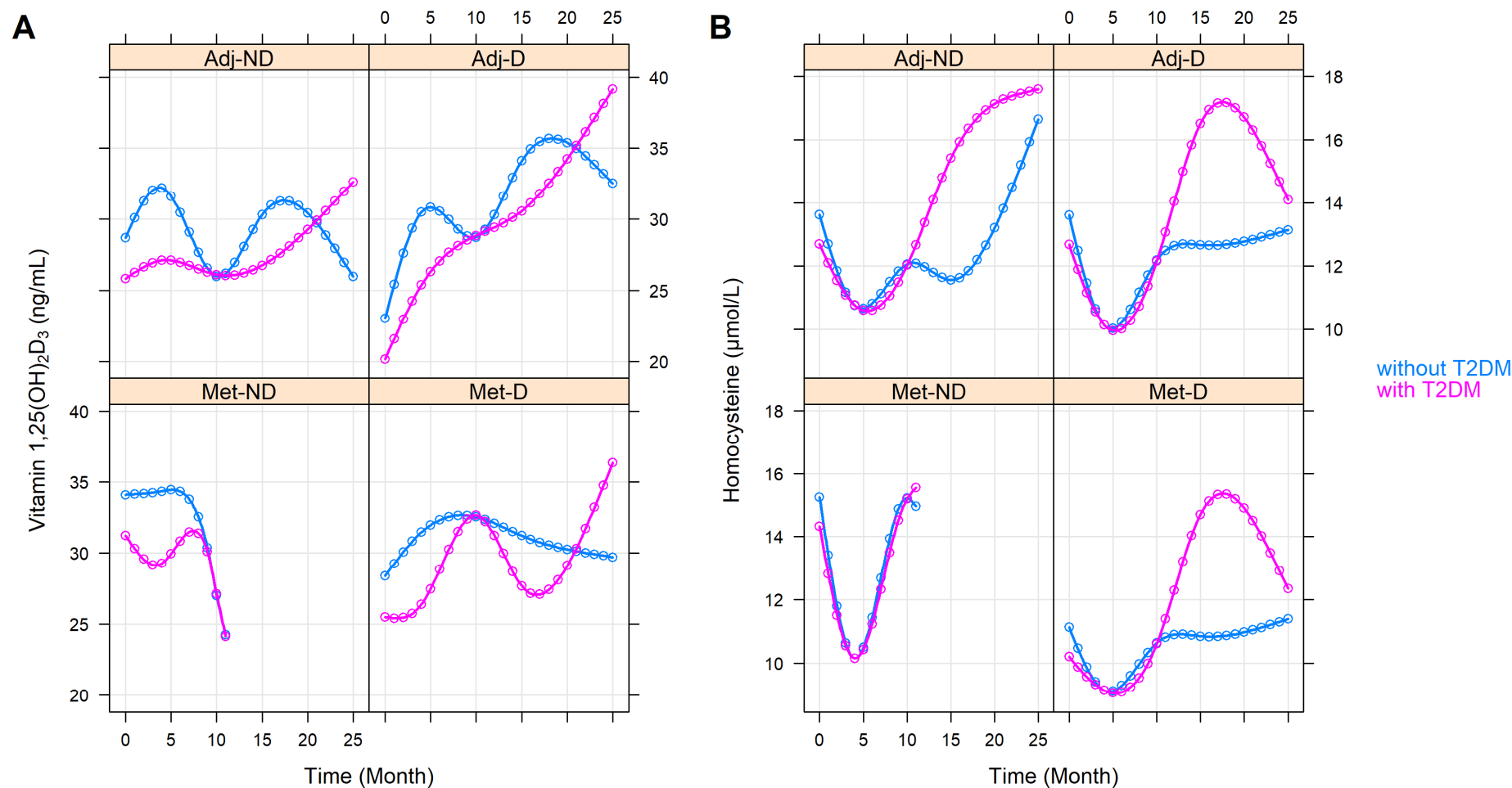
**Figure S3.** Predictions of average longitudinal changes in vitamin 1,25(OH)<sub>2</sub>D<sub>3</sub> (A) and homocysteine (B) level of the study groups throughout the first 25 months of the observation time, stratified by the presence of hypertension (HT). Adj-ND: patients without metastasis and no vitamin D<sub>3</sub> supplementation; Adj-D: patients without metastasis with vitamin D<sub>3</sub> supplementation; Met-ND: patients with metastasis and no vitamin D<sub>3</sub> supplementation; Met-D: patients with metastasis with vitamin D<sub>3</sub> supplementation.



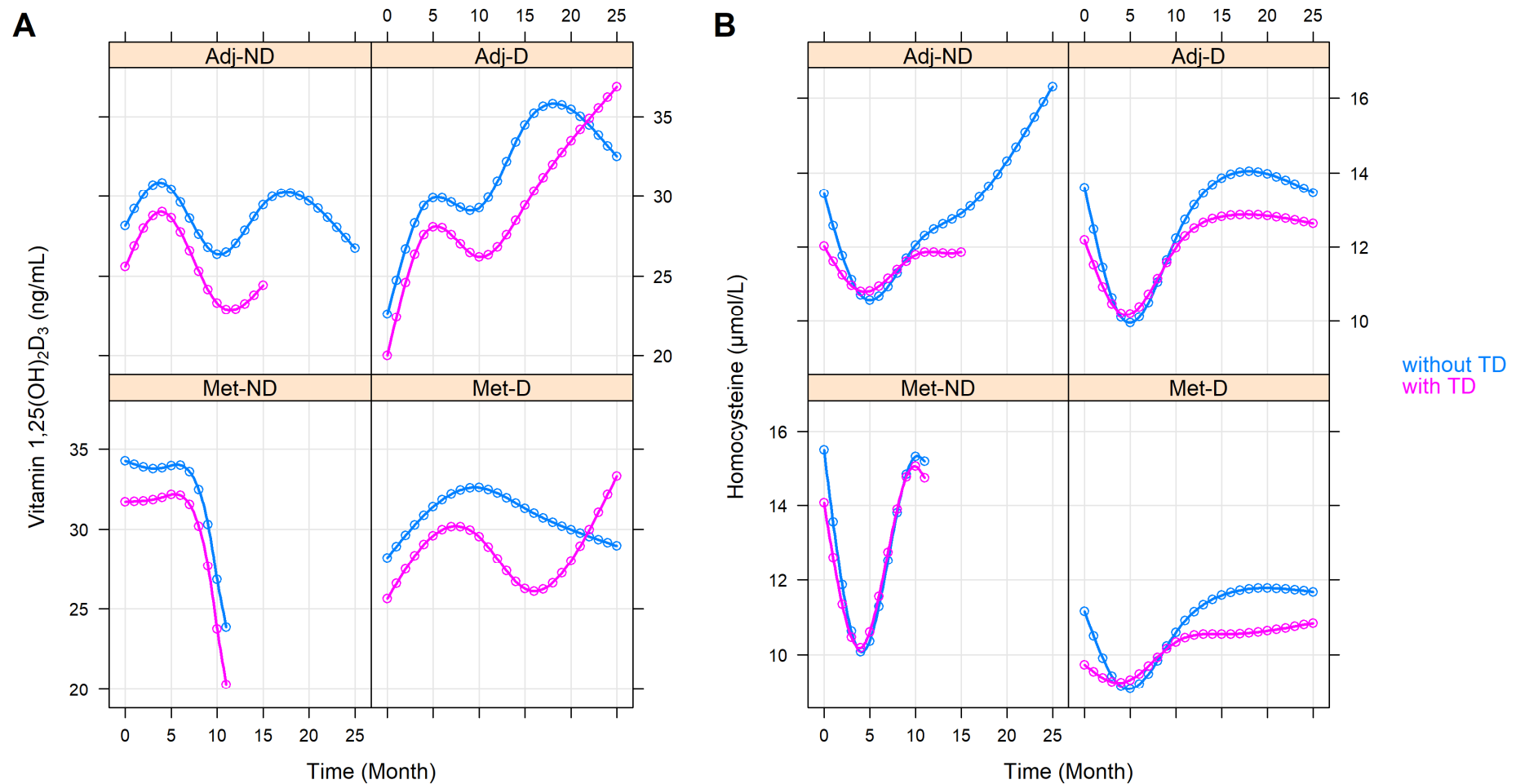
**Figure S4.** Predictions of average longitudinal changes in vitamin 1,25(OH)<sub>2</sub>D<sub>3</sub> (**A**) and homocysteine (**B**) level of the study groups throughout the first 25 months of the observation time, stratified by the presence of cardiovascular diseases (CVD) excluding previous major cardiovascular events (*e.g.* stroke, infarct, etc.) and hypertension. Adj-ND: patients without metastasis and no vitamin D<sub>3</sub> supplementation; Adj-D: patients without metastasis with vitamin D<sub>3</sub> supplementation; Met-ND: patients with metastasis and no vitamin D<sub>3</sub> supplementation; Met-D: patients with metastasis with vitamin D<sub>3</sub> supplementation.



**Figure S5.** Predictions of average longitudinal changes in vitamin 1,25(OH)<sub>2</sub>D<sub>3</sub> (**A**) and homocysteine (**B**) level of the study groups throughout the first 25 months of the observation time, stratified by the presence of previous cardiovascular events (CVE), such as stroke, myocardial infarct, *etc.* Adj-ND: patients without metastasis and no vitamin D<sub>3</sub> supplementation; Adj-D: patients without metastasis with vitamin D<sub>3</sub> supplementation; Met-ND: patients with metastasis and no vitamin D<sub>3</sub> supplementation; Met-D: patients with metastasis with vitamin D<sub>3</sub> supplementation.



**Figure S6.** Predictions of average longitudinal changes in vitamin 1,25(OH)<sub>2</sub>D<sub>3</sub> (A) and homocysteine (B) levels of the study groups throughout the first 25 months of the observation time, stratified by the presence of type 2 diabetes mellitus (T2DM). Adj-ND: patients without metastasis and no vitamin D<sub>3</sub> supplementation; Adj-D: patients without metastasis with vitamin D<sub>3</sub> supplementation; Met-ND: patients with metastasis and no vitamin D<sub>3</sub> supplementation; Met-D: patients with metastasis with vitamin D<sub>3</sub> supplementation.



**Figure S7.** Predictions of average longitudinal changes in vitamin 1,25(OH)<sub>2</sub>D<sub>3</sub> (**A**) and homocysteine (**B**) level of the study groups throughout the first 25 months of the observation time, stratified by the presence of any thyroid diseases (TD). *Note: patients who were not in an euthyroid state were excluded from the study.* Adj-ND: patients without metastasis and no vitamin D<sub>3</sub> supplementation; Adj-D: patients without metastasis with vitamin D<sub>3</sub> supplementation; Met-ND: patients with metastasis and no vitamin D<sub>3</sub> supplementation; Met-D: patients with metastasis with vitamin D<sub>3</sub> supplementation.