LETTER TO THE EDITOR

Cost-minimisation in vitamin B12 deficiencies: expensive diagnostics can reduce spending

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To the Editor,

The diagnostic approach to detect vitamin B12 deficiencies is centred around measuring plasma vitamin B12 concentrations, even though these do not always give a correct representation of the functional availability of vitamin B12. For example, markers of functional vitamin B12 deficiencies, such as methylmalonic acid (MMA), have been shown to be aberrant in only 30% of patients with low-normal vitamin B12 concentrations (between 100 and 200 pmol/l).[1] As such, guiding therapeutic intervention by MMA instead of vitamin B12 will prevent unnecessary treatment in patients with indecisive (low-normal) vitamin B12 concentrations, in whom B12 measurements are not conclusive in determining deficiencies.

In the Netherlands, treatment generally consists of intramuscular (IM) administration[2] of vitamin B12, although the clinical effectiveness of high-dose oral supplementation (OS) was shown in various prospective studies.[3,4] As a small amount (±1%) of vitamin B12 is absorbed by passive diffusion, without the mediation of intrinsic factor,[5] OS is also effective in patients with deficiencies in the active uptake of vitamin B12. Hereby, daily oral administration of 1000 μg of vitamin B12 is considered to be sufficient for treating deficiencies (reviewed by Andres *et al.*[6]).

To investigate which combination of diagnostic and therapeutic options for vitamin B12 deficiencies allows the lowest cost, and hence, the most efficient care provision, we applied a cost-minimisation analysis to a commonly used diagnostic flowchart (adapted from Wiersinga *et al.*[7]). The diagnostic flow chart and the resulting costs in the first year of treatment are shown in *figure 1*.

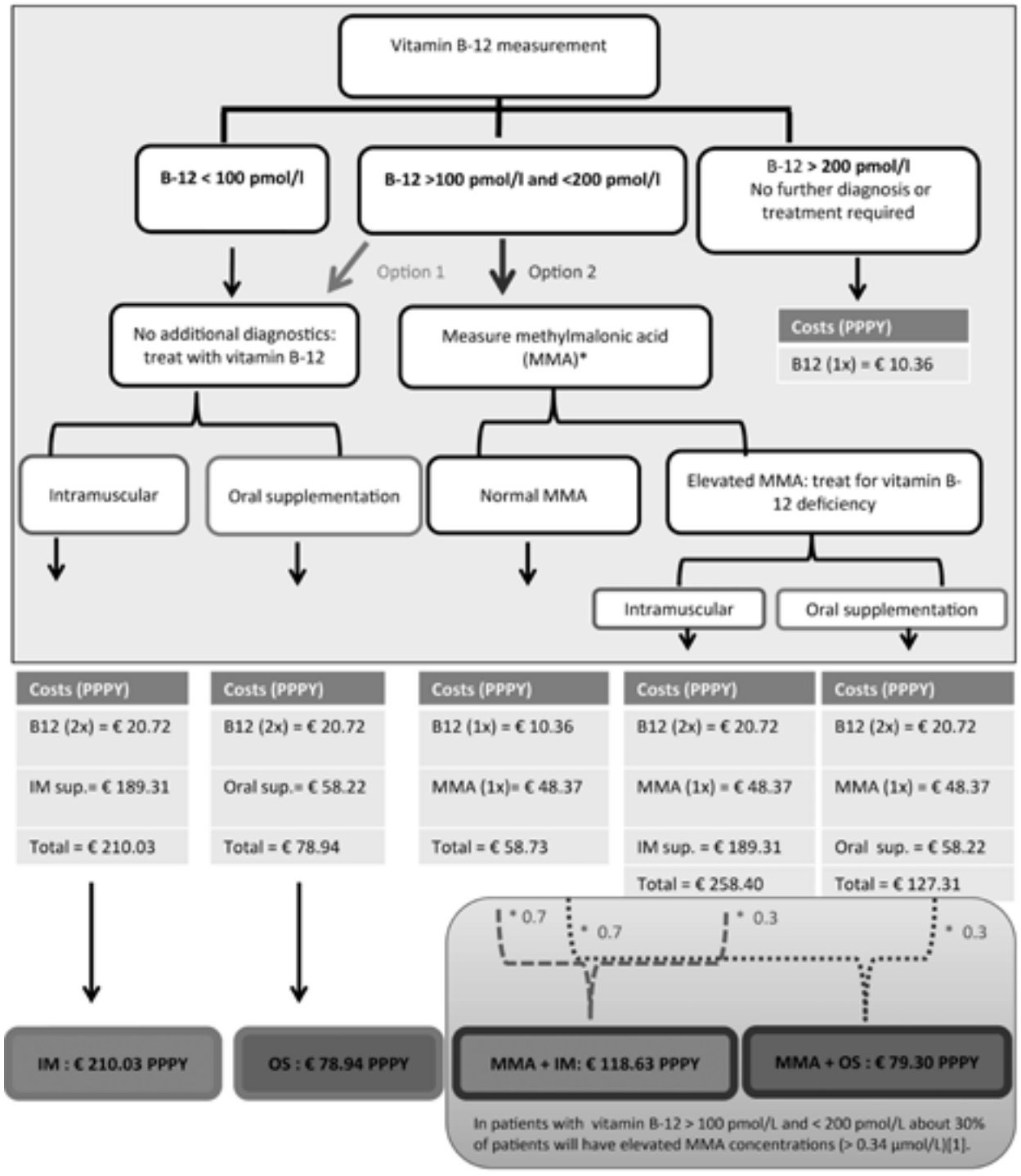
In patients with plasma vitamin B12 concentrations between 100 and 200 pmol/l, the MMA-guided IM treatment saves approximately € 91 per person per year in the first year of treatment (PPPY) compared with direct IM treatment. OS treatment enables the additional saving of approximately € 39 PPPY. Guiding OS by MMA prevents unnecessary treatments at roughly the same cost of direct OS.

In summary, the additional diagnostics prevent unnecessary treatment and our calculations present a clear example of how laboratory diagnostics can be used to improve both patient wellbeing and reduce healthcare spending. Moreover, the use of MMA analysis to guide the diagnosis and treatment of vitamin B12 deficiencies enables substantial reductions in costs. The greatest efficiency in care is obtained by combining MMA analysis and OS treatment. Unfortunately, Dutch health insurance companies only reimburse IM treatment. Time to reconsider their policy?

REFERENCES

1. Van den Ouweland JM, Beijers AM, Van Daal H. Diagnostische opbrengst van standaard reflexmeting op serum methylmalonzuur voor het vaststellen van een functioneel vitamine b12 tekort. Ned Tijdschrift Klin Chem Labgeneeskunde. 2011;36:263-4.
2. Wijk MAM, Mel M, Muller AP, Silverentand JGW, Pijnenborg L, Kolnaar MGB. Nhg-standaard anemie, nhg-standaarden voor de huisarts 2009. In: Wiersma T, Boukes FS, Geijer RMM, Goudswaard AN, eds.: Bohn Stafleu van Loghum; 2009:1277-90.
3. Bolaman Z, Kadikoylu G, Yukselen V, Yavasoglu I, Barutca S, Senturk T. Oral versus intramuscular cobalamin treatment in megaloblastic anemia: A single-center, prospective, randomized, open-label study. Clin Ther. 2003;25:3124-34.
4. Kuzminski AM, Del Giacco EJ, Allen RH, Stabler SP, Lindenbaum J. Effective treatment of cobalamin deficiency with oral cobalamin. Blood. 1998;92:1191-8.
5. Berlin H, Berlin R, Brante G. Oral treatment of pernicious anemia with high doses of vitamin b12 without intrinsic factor. Acta Med Scand. 1968;184:247-58.
6. Andres E, Fothergill H, Mecili M. Efficacy of oral cobalamin (vitamin b12) therapy. Expert Opin Pharmacother. 2010;11:249-56.
7. Wiersinga WJ, de Rooij SE, Huijmans JG, Fischer C, Hoekstra JB. [diagnosis of vitamin b12 deficiency revised]. Ned Tijdschr Geneeskd. 2005;149:2789-94.

Figure 1. *Diagnosis of vitamin B12 deficiencies and the associated costs per person per year (PPPY) in the first year of treatment. Costs taken into account are: laboratory analysis of MMA and vitamin B12, vitamin B12 medication (IM or OS), pharmacy dispensing fee and administration of injections (by general practitioner). Costs and resources were gathered from the rates published in 2011 or 2012 by the Dutch Healthcare Authority (www.nza.nl)*



Assumptions: IM treatment consists of 10 injections in the first months, followed by 1 injection every 2 months (as advised by the Dutch college of General Practitioners).[2] OS treatment consists of 1 (1000 µg) vitamin B12 tablet per day.[6] Costs of vitamin B12 tablets for OS treatment: 100 tablets (1000 µg each) € 15.95 (obtained from an internet search, this price seems representative for online and offline alternatives)