

# Sex differences in B12 opinions

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*Objective* -To elucidate possible sex differences in knowledge, competence, and attitudes behind decision-making on B12-associated problems.

*Design* - Postal questionnaire study.

*Setting*- Swedish national samples.

*Subjects* - Random samples of general practitioners (1996, 1998), and a total sample of all geriatricians (1998). The over-all response rate was 71%. The study group comprised 480 female physicians and 526 male physicians.

*Main outcome measures* - The responses to 24 statements in a postal questionnaire were measured by means of visual analogue scales. Group differences were evaluated by medians and shapes of distributions.

*Results* -The female doctors appeared to value patient-related symptoms and signs more than male doctors. Conversely, male doctors relied on laboratory tests more than female doctors. As reflected by questionnaire answers, female doctors appeared to have more skill and knowledge than male doctors do on B12-associated clinical problems.

*Conclusions* - The observations were compatible with the hypothesis that female Swedish doctors were more informed on B12-associated clinical problems than males in the period 1996-98.

*Key words:* Vitamin B12, deficiency, diagnosis, management, attitudes, gender

## INTRODUCTION

All scientists and all physicians with interest in B12-associated problems are aware of pitfalls in the diagnosis of deficiency states. The post-doctoral education in the field has hitherto been a classical top-down approach – experts have told the clinicians in charge of most patients how to think and behave.

Instead of the signals sent, the present study focused on the signals accepted by receiving physicians in two main receptor groups. The pattern of acceptance was significantly influenced by the gender of the responders - the concepts “sex” and “gender” are used interchangeable. Thus, the aim of the study was to describe sex differences of knowledge, competence, and attitudes behind decision-making on B12-associated clinical problems.

## SUBJECTS AND METHODS

### *Study population and sampling*

The study population and sampling were described in detail in previous papers (1,2). Detail information on the comparison between GPs and geriatricians 1998 is available as electronic preprint (reference 4 in Rondel 2000; 3: Editorial, / [www.rondellen.net/](http://www.rondellen.net/)).

Questionnaires were posted August-December 1996 and 1998 to a representative sample of Swedish general practitioners (GPs), randomised and stratified according to zip code. In addition, all Swedish geriatricians were questioned in the same period 1998.

The GPs questioned 1996 were excluded 1998 prior to randomisation in order to avoid questionnaire overloading and questionnaire training. The study group then comprised 480 female physicians and 526 male physicians.

### *Questionnaires, response rates, and sex ratios*

The questionnaire contained 24 statements to be evaluated by a visual-analogue scale (Tables 1 - 6). The response rates were 74%, 70% and 69%. The female to male ratio was 6 - 4 in the geriatrician group, and 4 - 6 in the GP groups.

### *Grouping of adjacent categories*

The B12 opinions were stable with marginal shifts in the GP group over the time period 1996-98. The numerical differences between GPs and geriatricians were marginal in 1998. It was thus deemed reasonable to regard GPs 1996, GPs 1998 and geriatricians 1998 as adjacent categories and group the answers together for the

study of sex and gender differences (3).

### Statistical analysis

Possible sex differences were evaluated by the Mann-Whitney two-sample test regarding changes around the median value, by the Cramer-von Mises test regarding changes of distribution shape.

## RESULTS

### Responders and non-responders

In the total material (Tables I-VI), there was no obvious difference by age and sex between responders and non-responders. The over-all response rate was 71%.

### Clinical skill and knowledge

Statements No 1-6 probed clinical skill and knowledge (Table 1). Women doubted the statement that vitamin B12 deficiency is nowadays entirely a laboratory diagnosis. Women were also more certain than men that vegans, anorectics and elderly are risk groups for vitamin B12 deficiency.

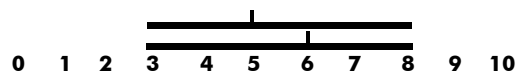
**Table 1.** Test of differences between female and male doctors in the evaluation of statements 1- 6.

Endpoints of lines are 25<sup>th</sup> and 75<sup>th</sup> percentile. The vertical line is the median. Top line is female and bottom line is male doctors.

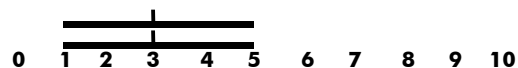
1 "Anamnesis and physical examination are essential in investigating and treating a case of suspected vitamin B12 deficiency!" (479/526<sup>α</sup>) *MW=ns, CvM=ns*



2 "Vitamin B12 deficiency is nowadays entirely a laboratory diagnosis!" (475/523<sup>α</sup>) *MW=0.03, CvM<0.05*



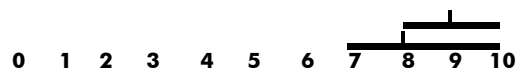
3 "Women in fertile age are a risk group for vitamin B12 deficiency!" (458/509<sup>α</sup>) *MW=ns, CvM=ns*



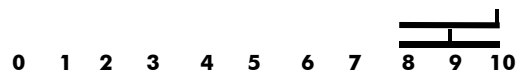
4 "Vegans are a risk group for vitamin B12 deficiency!" (472/516<sup>α</sup>) *MW<0.001, CvM<0.01*



5 "Anorectics are a risk group for vitamin B12 deficiency!" (476/518<sup>α</sup>) *MW<0.001, CvM<0.01*



6 "Persons above 70 years of age are a risk group for vitamin B12 deficiency!" (480/524<sup>α</sup>) *MW<0.001, CvM<0.01*

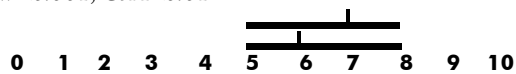


<sup>α</sup> (Number of female evaluations / number of male evaluations)

### Knowledge and application

Statements No 7 and No 19 tested basic knowledge and clinical application (Table 2). Women were more convinced that alcoholics often have a functional vitamin B12 deficiency despite normal levels of serum cobalamins. Concerning the underlying knowledge – functional vitamin B12 deficiency may occur despite normal or even high levels of serum cobalamins – there was no sex difference.

**Table 2.** Test of differences between female and male doctors in the evaluation of statements 7 and 19. Endpoints of lines are 25<sup>th</sup> and 75<sup>th</sup> percentile. The vertical line is the median. Top line is female and bottom line is male doctors.  
 7 “In alcoholics, serum cobalamin is often normal despite a functional vitamin B12 deficiency!” (425/476 <sup>α</sup>)  
*MW*<0.001, *CvM*<0.01



19 “Functional vitamin B12 deficiency may occur despite normal or high serum cobalamin” (462/514 <sup>α</sup>)  
*MW*=ns, *CvM*=ns



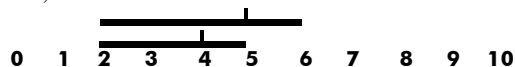
$\alpha$  (Number of female evaluations / number of male evaluations)

### Clinical accuracy

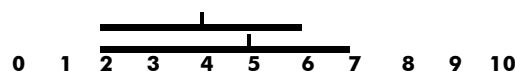
The evaluations probed by statements No 8-10 and 24 (Table 3) suggested, that women were more inclined than men to favour clinical picture instead of laboratory tests. The present gender difference corresponded to the group responses to statement No 2 (Table 1).

**Table 3.** Test of differences between female and male doctors in the evaluation of statements 8 - 10 and 24. Endpoints of lines are 25<sup>th</sup> and 75<sup>th</sup> percentile. The vertical line is the median. Top line is female and bottom line is male doctors.

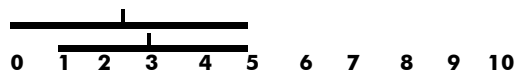
8 “A competent clinician does not need many laboratory tests to find his cases of vitamin B12 deficiency. Every fifth patient investigated for suspected vitamin B12 deficiency has, in fact, vitamin B12 deficiency!” (451/497 <sup>α</sup>)  
*MW*=ns, *CvM*=ns



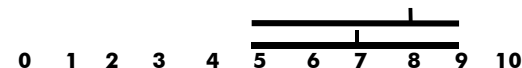
9 “Serum cobalamin and serum folate are valuable but, unfortunately, capricious markers for many different sorts of malnutrition and malabsorption. It is acceptable that only every 10<sup>th</sup> investigation demonstrates deficiency of vitamin B12!” (439/495 <sup>α</sup>) *MW*=ns, *CvM*<0.05



10 “Serum cobalamin and serum folate are valuable but, unfortunately, capricious markers for many different sorts of malnutrition and malabsorption. It is acceptable that only every 20th investigation demonstrates deficiency of vitamin B12!” (417/483 <sup>α</sup>) *MW*=0.01, *CvM*<0.01



24 “It is still acceptable to treat a patient with obscure neuropathy with vitamin B12 during 6-36 months and evaluate treatment efficiency by clinical parameters (e.g. performance, walking distance, reappearance of vibration sense or reflexes, reduction of sensory loss, reduction of hair loss, reduction of muscular pain!)” (455/513 <sup>α</sup>)  
*MW*=ns, *CvM*=ns



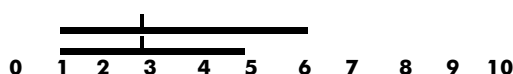
$\alpha$  (Number of female evaluations / number of male evaluations)

### Classical markers and new markers

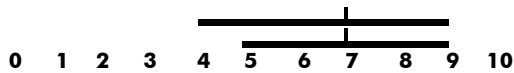
Statements No 11-14 tested the attitudes to classical markers and new markers for vitamin B deficiency (Table 4). The responders appeared to accept the new markers for vitamin B deficiency, methylmalonic acid and homocysteine, but were not ready to accept homocysteine as the first screening test for vitamin B12 and/or folate deficiency. The shape of the distributions suggested a minor gender difference in the evaluation of serum gastrin versus the Schilling test.

**Table 4.** Test of differences between female and male doctors in the evaluation of statements 11 - 14. Endpoints of lines are 25<sup>th</sup> and 75<sup>th</sup> percentile. The vertical line is the median. Top line is female and bottom line is male doctors.

11 “Homocysteine in serum or plasma replaces entirely serum cobalamin and serum folate in the first laboratory screening of a suspected case of malnutrition or malabsorption!” (453/495 <sup>α</sup>) *MW*=ns, *CvM*=ns

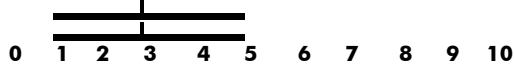


12 "A meticulous clinician cannot do without serum methyl malonate when investigating a case of suspected vitamin B12 deficiency!" (463/509<sup>α</sup>) *MW=ns, CvM=ns*



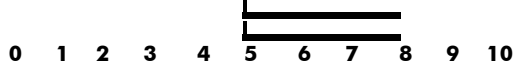
13 "The clinical significance of the modern markers homocysteine and methyl malonate in cases of suspected vitamin B12 deficiency is overrated!" (461/505<sup>α</sup>)

*MW=ns, CvM=ns*



14 "Serum gastrin, fasting value, is cheaper and more easy to interpret than the Schilling test in cases of suspected vitamin B12 malabsorption!" (388/409<sup>α</sup>)

*MW=ns, CvM<0.05*



$\alpha$  (Number of female evaluations / number of male evaluations)

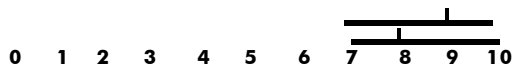
### Pitfalls in routine laboratory diagnosis

Statements No 15-18 probed some classical pitfalls in routine laboratory testing for vitamin B12 deficiency (Table 5). On a high level of professional knowledge, the female team scored 2-1 against the male team.

**Table 5.** Test of differences between female and male doctors in the evaluation of statements 15 - 18. Endpoints of lines are 25<sup>th</sup> and 75<sup>th</sup> percentile. The vertical line is the median. Top line is female and bottom line is male doctors.

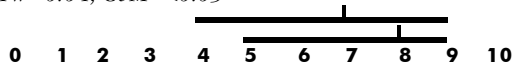
15 "Simultaneous deficiency of iron and deficiency of vitamin B12 may produce an anaemia with normal MCV (mean corpuscular volume)!" (456/498<sup>α</sup>)

*MW=ns, CvM<0.05*

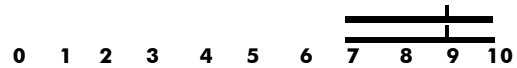


16 "Treatment with vitamin B12 may turn a macrocytic anaemia into a microcytic anaemia!" (432/502<sup>α</sup>)

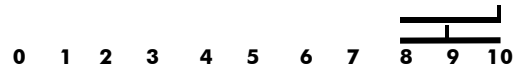
*MW=0.04, CvM=<0.05*



17 "It is an error of the art to treat a macrocytic anaemia with folate only!" (459/503<sup>α</sup>) *MW=ns, CvM=ns*



18 "Functional vitamin B12 deficiency in cells and tissues may occur despite normal or high blood haemoglobin!" (471/514<sup>α</sup>) *MW<0.001, CvM<0.05*



$\alpha$  (Number of female evaluations / number of male evaluations)

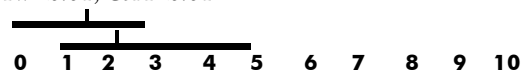
### Prophylactic therapy in malabsorption

Atrophic gastritis and surgical procedures in the stomach are prone to impair the absorption of vitamin B12. Statements No 20-23 probed attitudes to prophylactic B12 therapy to such patients (Table 6). Female doctors appeared to accept prophylactic B12 therapy in the risk groups mentioned

**Table 6.** Test of differences between female and male doctors in the evaluation of statements 20 - 23. Endpoints of lines are 25<sup>th</sup> and 75<sup>th</sup> percentile. The vertical line is the median. Top line is female and bottom line is male doctors.

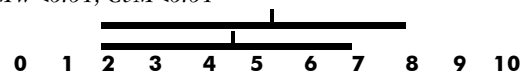
20 "There is no reason to substitute patients with atrophic gastritis with vitamin B12!" (468/520<sup>α</sup>)

*MW<0.01, CvM<0.01*



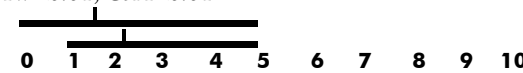
21 "As a precaution, I prescribe vitamin B12 to all my patients with atrophic gastritis!" (452/506<sup>α</sup>)

*MW<0.01, CvM<0.01*



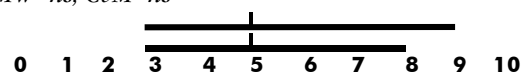
22 "There is no reason to substitute patients with vitamin B12 after gastric surgery!" (461/500<sup>α</sup>)

*MW<0.01, CvM<0.01*



23 "As a precaution, I prescribe vitamin B12 to all patients with gastric resections!" (450/490<sup>α</sup>)

*MW=ns, CvM=ns*



$\alpha$  (Number of female evaluations / number of male evaluations)

more than male doctors. However, the numerical differences were small.

## **DISCUSSION**

### *Principal findings*

The present results suggested subtle but statistically significant sex differences in attitudes towards B12-associated clinical problems. The crop of statistical stars in Tables 1 - 6 deviated significantly from that expected under the null hypothesis (25/48 < 0.05, chi-square test  $p < 0.001$ ).

### *Strengths and weaknesses of the study*

The internal structure of the statements of the present questionnaire was complex (Tables 1 -6). For purposes of analysis, it is reasonable to categorise them in matter-of-fact statements, matter-of-mind statements, and matter-of-debate statements. It is conceivable that the grouping of a statement may be subject to discussion.

On the matter-of-fact level, both female doctors and male doctors strayed in the evaluation of statement No 3 (Table 1); a population-based study in a post-industrial society documented that women in fertile age

provide a risk group for vitamin B12 deficiency (4). Other risk groups (vegans, anorectics, elderly, alcoholics) were properly identified by most doctors with a plus for female physicians. Furthermore, classical pitfalls in routine laboratory diagnosis of vitamin B12 deficiency were properly recognised by most doctors (Table 5).

On the matter-of-mind level, female doctors appeared to rely more on the patient than on the laboratory tests, as compared with male doctors. The interpretation is based on evaluations of statements No 1-2, 8-10, and 24. In support of this view, female doctors appeared to be more active than male doctors in treating patients with suspected B12 malabsorption (Table 6) are. However, it should be emphasised that group differences were small with risks for over-interpretation.

On the matter-of-debate level, the evaluation of new and classical markers of vitamin B12 deficiency did not reveal any certain sex difference (Table 6). It is reasonable to assume that the intense scientific debate on the subjects (5,6) hampered the formation of clinical opinions. However, most of the participants accepted the view that homocysteine and methylmalonic acid are valuable markers for vitamin B12 deficiency (7-9)

### *Strength and weakness in relation to other studies*

To our knowledge, there is no previous study on sex differences of B12 opinions. However, an ancient tradition common to cultures with Jew, Christian and Islam roots implies that man and woman provide two halves of one entity. "So God created man in his own image, in the image of God he created him; male and female he created them" (10).

In addition to tradition, genus research suggests that the two halves of man are not equal from biological, economical, and social points of view. The present study represents an extension of gender research to B12-associated clinical and laboratory problems.

### *Meaning of the study*

It should be emphasised that the responses in the present study reflected a high degree of knowledge and professional competence. The group differences between the sexes were marginal from a numerical point of view and of doubtful clinical importance. Nevertheless, it is difficult to avoid the conclusion that female doctors were more informed than male doctors on

B12-associated clinical problems in the setting studied.

### *Unanswered questions*

Since the study was carried out in Sweden 1996-98, the results may not apply to physicians of other times and countries.

### ACKNOWLEDGEMENTS

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### *Announcement*

As a GP you will learn from our paper that knowledge and attitudes of B12-associated problems were influenced by gender in Swedish physicians 1996-98.