# Laboratoriumtesten in de huisartsgeneeskunde

*KCE reports 59A*

Federaal Kenniscentrum voor de Gezondheidszorg
Centre fédéral d'expertise des soins de santé
2007

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# VOORWOORD

Laboratorium testen zijn onmisbaar geworden in de geneeskunde van vandaag. Meerdere testen vormen een onmiskenbare vooruitgang in de diagnose en de opvolging van ziekte of behandeling. Mede als een gevolg hiervan is hun gebruik de laatste decennia gestaag toegenomen.

In het letterlijke gros aan individuele testen waarover een aanvragende arts beschikt, is het niet altijd eenvoudig om het bos nog door te bomen te zien en te weten welke test voor welke situatie best geschikt is. De patiënt kan negatieve gevolgen ondervinden van het verkeerd of onnodige aanvragen van labotesten. Vals positieve resultaten geven aanleiding tot bijkomende testen en/of overbodige behandelingen. Eerdere studies tonen dat onnodige testen kunnen leiden tot een lagere patiëntentevredenheid. Aan de andere kant worden testen soms onterecht niet aangevraagd, waardoor de patiënt sub-optimale zorg krijgt.

Laboratoriumtesten zijn elk apart niet duur, maar hun totale kost is aanzienlijk. In een tijdperk waarin de nood aan medische zorg toeneemt, stijgt ook de vraag naar doelmatigheid. Op zich zijn er weinig stimuli die voorschrijvers van labo-testen aanzetten tot een rationeel gebruik ervan. Een recente omzendbrief van de Commissie Klinische Biologie trok hard van leer tegen sommige labo's die aan voorschrijvers voordelen geven die al lang niet meer als een "normaal" relatiegeschenk kunnen beschouwd worden.

Voor dit rapport werden prospectieve data verzameld om een gedetailleerde analyse toe te laten van het aanvraaggedrag van huisartsen. Die inzameling was onmogelijk geweest zonder de welwillende medewerking van meerdere klinisch biologen en aanvragende artsen. Daarnaast werden ook mogelijke interventies om goed aanvraaggedrag te ondersteunen bestudeerd. En of de gewoonte van klachtenvrije personen om naar de huisarts te gaan 'om eens bloed te pakken' zinvol is, ook dat kan u in dit rapport terugvinden.

Jean-Pierre CLOSON
Adjunct algemeen directeur

Dirk RAMAEKERS
Algemeen directeur

# EXECUTIVE SUMMARY

## INTRODUCTIE

Het belangrijkste doel van dit rapport was om het gebruik van laboratoriumtesten in de huisartspraktijk te beschrijven, en methoden te exploreren die het test aanvraaggedrag kunnen verbeteren.

## HUIDIGE PRAKTIJK

Algemeen gesteld stijgt het gebruik van laboratoriumtesten, hoewel sommige testen minder gebruikt worden. Stollingstesten vertoonden de grootste relatieve stijging: van 1.500.000 testen per jaar in 1995 naar 3.500.000 testen per jaar in 2005.

Patiënten die minstens 3 maanden per jaar medicatie namen hadden kortere intervallen tussen twee laboratoriumtesten dan patiënten die dat niet deden, met een mediaan van 3,9 versus 6,5 maanden. Er waren ook kortere intervallen bij patiënten met langere hospitalisatieduur. Nochtans zijn de verschillen in absolute getallen niet groot.

## GEPAST GEBRUIK VAN LABORATORIUMTESTEN IN DE HUISARTSPRAKTIJK

### DEFINITIE VAN GEPAST GEBRUIK

Een systematisch literatuuroverzicht leverde 317 artikels op. Na het toepassen van inclusie en exclusiecriteria bleven er uiteindelijke negen artikels over. Vier van deze artikels gebruikten richtlijnen als criterium voor gepast aanvraaggedrag. Twee artikels gebruikten expert opinie. Een artikel gebruikte setting-specifieke studies voor diagnostische testkarakteristieken; de laatste twee artikels specificeerden geen criteria voor gepast aanvraaggedrag, hoewel één artikel wel een algoritme gebruikte voor schildkliertesten.

Hieruit kan men besluiten dat richtlijnen het meest gebruikte criterium voor gepast aanvraaggedrag zijn.

### SYNTHESE VAN BESTAANDE RICHTLIJNEN

Aanbevelingen over laboratoriumtesten van 118 verschillende richtlijnen warden gesynthetiseerd. De meeste richtlijnen werden ontwikkeld voor een aandoening of syndroom, en bevatten slechts enkele paragrafen over laboratoriumtesten. Slechts één richtlijn werd speciaal gemaakt voor laboratoriumtesten in de huisartsgeneeskunde, door het NHG samen met de Nederlandse vereniging voor Klinische Chemie en SAN.

Hemoglobine werd het meeste aanbevolen, namelijk voor 35 verschillende indicaties. Creatinine werd aanbevolen voor 22 verschillende indicaties; glucose voor 18 indicaties. Sommige testen die in België frequent gebruikt worden werden in geen enkele richtlijn aanbevolen, bijvoorbeeld chloride en fibrinogeen.

Levels of evidence of grades of recommendation werden maar bij 24 indicaties aangegeven.

# PROSPECTIEVE STUDIE IN DE HUISARTSPRAKTIJK

Huisartsen (n=164) werden gerecruteerd voor de studie via 5 private laboratoria, resulterend in 1579 labo test aanvraagformulieren. Voor elk aanvraagformulier werd gevraagd naar de reden om labotesten aan te vragen, en meer specifiek om een bepaalde test te vragen: uitsluiten van een aandoening, bevestigen van een diagnose, follow-up, op vraag van de patiënt, etc.

De gemiddelde leeftijd van de patiënten was 58.2 jaar (SD 20.1) met 44.7% mannen. Gemiddeld werden er 13.3 testen aangevraagd per formulier. De gemiddelde Totale kost per order was 39.4€, waarvan de patiënt 7.3€ zelf moet betalen. In 18% van de aanvragen werd enkel PT/INR aangevraagd. Als deze aanvragen werden uitgesloten, was het gemiddelde testen per aanvraag 16.2 met een totale kost van 44.1€ en 9.1€ voor de patiënt.

De 10 meest frequent aangevraagde testen waren: Hb, RBC+Hct, WBC, WBC formule, AST+ALT, creatinine, glucose, plaatjes, gamma-GT en totale cholesterol.

De voornaamste reden om labotesten aan te vragen was voor de follow-up van een chronische aandoening of behandeling (55.5%). In 20% van de gevallen was diagnostiek de belangrijkste redden, en ongeveer 10% werd aangevraagd voor algemene check-up or preventie. Andere redenen zoals 'op vraag van de patiënt' (4%) of 'op vraag van een specialist' (0.4%) waren veel minder frequent. Daarbij hadden huisartsen in bijna de helft van de gevallen (45%) nog minstens 1 bijkomende reden: één bijkomende reden in 34%; twee bijkomende redenen in 9,4% en drie redenen in 22 gevallen.

De vier meest frequente algemene redenen om labotesten aan te vragen werden in meer detail bestudeerd en vergeleken met de richtlijnen: algemene check-up/preventie, diabetes, hypertensie en zwakte/algemene moeheid. (tabel 1)

Voor elke indicatie wordt het aantal aanvragen gegeven (1$^{e}$ kolom), de proportie hiervan waarvoor het de enige reden tot aanvragen was (2$^{e}$ kolom) en de proportie met bijkomende redenen (3$^{e}$ kolom). Vervolgens wordt het aantal aanbevolen testen volgens de richtlijnen voor die indicatie gegeven, en de aanbevolen testen wanneer ook bijkomende redenen in acht worden genomen (4$^{e}$ kolom). Tenslotte wordt de proportie ongepaste testen berekend: testen worden als gepast beschouwd als ze worden aanbevolen door de richtlijnen voor die indicatie of voor mogelijke bijkomende redenen. Daarbij wordt er ook vanuit gegaan dat die testen gepast waren waarvoor de huisarts nog een specifieke andere reden heeft opgegeven. (laatste kolom)

Bijkomend werd een financiële analyse gemaakt voor elke indicatie: de totale kost voor alle aanvragen, de kost per aanvraag en de persoonlijke bijdrage van de patiënt. Vervolgens werden de kosten berekend indien de richtlijnen gevolgd waren voor die indicatie, voor die indicatie en de bijkomende redenen, en tenslotte met de testen waarvoor nog een andere specifieke reden werd gegeven. (Zie tabel 2)

Naast de analyse van deze vier indicaties werden ook enkele individuele testen van naderbij bekeken, namelijk enkele testen die frequent werden aangevraagd maar waarvoor weinig indicaties werden terug gevonden. Deze analyses staan in tabel 3.

**Tabel 1: redenen om laboratoriumtesten aan te vragen, en vergelijking met de richtlijnen**

| | Aanvragen N | Aanvragen met één reden % | Aanvragen met bijkomende redenen % | Aantal testen N (SD) | Aanbevolen testen n | Niet aanbevolen testen % | Ongepaste testen % |
|---|---|---|---|---|---|---|---|
| **Algemene check-up/preventie** | 155 | 16 | 54% follow-up<br>25% vraag patiënt<br>10% diagnostisch | 21 (6.1) | 6-14 | 46 | 38 |
| **Diabetes non insulin dependent** | 205 | 17 | 76% follow-up<br>11% diagnostisch<br>12% therapeutische monitoring | 13.5 (9.2) | 9-18 | 62.1 | 39.8 |
| **Hypertensie** | 184 | 11 | 76% follow-up<br>17% diagnostisch<br>7% therapeutische monitoring | 17.2 (8.1) | 8-12 | 66 | 59.6 |
| **Zwakte/algemene moeheid** | 121 | 0 | 25% follow-up<br>54% diagnostisch<br>10% vraag patiënt | 19 (6.9) | 6 | 74 | 44 |

**Tabel 2: financiële analyse**

| | Totale kost € | Kost/aanvraag € (SD) | Kost voor patiënt € (SD) | Kost/aanvraag aanbevolen testen € | Kost/aanvraag Aanbevolen + bijkomende redenen € | Kost/aanvraag Aanbevolen + bijkomende redenen + specifieke redenen € |
|---|---|---|---|---|---|---|
| **Algemene check-up/preventie** | 7770 | 50 (8) | 11.5 (2.6) | 24.4 | 41.6 | 44.3 |
| **Diabetes non insulin dependent** | 6897 | 45.4 | 7.1 (5.4) | 40.4 | 42.6 | 43.4 |
| **Hypertensie** | 8759 | 47.6 (12.7) | 9 (5) | 24.2 | 41.4 | 42.4 |
| **Zwakte/algemene moeheid** | 5985 | 49.4 (9.5) | 11 (23.4) | 24.4 | 24.4 | 41.3 |

**Table 3: selectie individuele testen**

| | Frequentie % | Belangrijkste reden om labotesten aan te vragen | Specifieke reden om deze test aan te vragen | Proportie van ongepaste aanvragen % |
|---|---|---|---|---|
| **Ureum** | 25.3 | 40% follow-up<br>26% diagnostisch | 50% screening<br>40% klinische redenen: nieraandoening, diabetes en monitoring diuretica | 87 |
| **Totaal eiwit** | 17.5 | 33% follow-up<br>29% diagnostisch<br>29% check-up/preventie | 70% screening<br>19% diagnostisch: inflammatie en voedingsdeficiëntie | 100 |
| **Amylase** | 13.7 | 31% follow-up<br>29% diagnostisch<br>26% check-up/preventie | 70% screening<br>26% diagnostisch: pancreas of chronisch alcohol misbruik | 77.5 |
| **Plaatjes** | 52.8 | 38% follow-up<br>28% diagnostisch<br>16% check-up/preventie | 80% screening<br>7% therapeutische monitoring of diagnostisch | 95 |
| **Chloride** | 16.7 | 42% follow-up<br>23% diagnostisch<br>20% check-up/preventie | 42% screening<br>43% therapeutische monitoring of diagnostisch (electrolieten stoornis) | 100 |

# INTERVENTIES OM TEST AANVRAAGGEDRAG IN DE HUISARTSPRAKTIJK TE BEÏNVLOEDEN

Een systematisch literatuuroverzicht identificeerde een goede systematische review die werd aangevuld met 12 originele studies.

In de systematische review werd een verminderd aantal of verminderde kost teruggevonden in 76% van de studies. Interventies gericht op meerdere gedragsfactoren waren meer succesvol (88%) dan studies gericht op één enkele factor (62%). De interventies gebruikten een variabele combinatie van LOK groep discussies, audit en feedback, het verspreiden van aanbevelingen, geheugensteuntjes, verantwoording voor bepaalde aanvragen en veranderingen aan het aanvraagformulier.

## Implementatie van aanbevelingen en feedback

Twee studies evalueerden een gecombineerde strategie waarin aanbevelingen gebruikt werden als basis voor feedback. Een studie vond geen effect op het aantal aangevraagde testen, terwijl de andere studie een daling met 5% terugvond.

In een RCT bespraken huisartsen hun persoonlijke feedback gerelateerd aan 3 EBM aanbevelingen in LOK groepen. Er was een significante daling ($p<0,05$) in het aantal testen met 12% in de ene groep, terwijl er in de andere interventiegroep geen significante daling optrad (8% versus 3% in de controle groep; $p = 0,22$).

De interventiegroep van een cluster RCT met feedback en korte geheugensteuntjes vroeg significant minder testen aan dan de controle groep: de odds ratio voor feedback was 0.87 (95%CI 0.81 - 0.94), de odds ratio voor geheugensteuntjes was 0.89 (95%CI 0.83 - 0.93), de odds ratio voor de combinatie van feedback en geheugensteuntjes was 0.78 (95%CI 0.71 - 0.85).

Een langdurige interventie van 9 jaar in Maastricht, bestaande uit 6-maandelijkse persoonlijke feedback gebaseerd op aanbevelingen, bereikte een daling met 45% voor 44 veel gebruikte testen van 1984 tot 1993 (gemiddelde jaarlijkse daling 6%, $p<0,01$). De controle groep had in diezelfde periode een jaarlijkse stijging met 3,2%.

## Elektronische besliskundige ondersteunende systemen

Een RCT vergeleek de doeltreffendheid van twee elektronische systemen. Een groep gebruikte een beperkt aanvraagformulier en de andere een beperkt formulier gebaseerd op aanbevelingen. De laatste groep vroeg 20% minder testen aan dan de eerste groep ($p<0.003$).

## Veranderingen aan aanvraagformulier

In een RCT verminderde het aantal testen met 18% na het invoeren van een beperkt aanvraagformulier, maar deze daling ging verloren nadat het oorspronkelijke formulier opnieuw werd ingevoerd ($p<0.001$). Smithuis bereikte ook een significante daling in het aanvragen van 3 testen (op een totaal van 6) door het gebruik van een beperkt formulier. In een andere studie bereikte een beperkt formulier gecombineerd met 6-maandelijkse feedback een vermindering van 23% op basis van een voor en nameting. Gelijkaardige resultaten werden ook gerapporteerd door Bailey et al. in het Verenigd Koninkrijk.

### Financiële interventies

In een Canadese retrospectieve studie werden 3 interventies gecombineerd: aanbevelingen, veranderd aanvraagformulier en wijzigingen aan de financiering (totaal thyroxine werd niet meer terugbetaald). Deze studie toonde een daling van 58% voor ureum testen en een daling van 80% voor ijzer.

In een studie in Nieuw-Zeeland mochten huisartsen de opbrengst van een daling van laboratorium testen gebruiken voor andere aspecten van hun praktijkvoering. Deze interventie leverde een daling in de kosten van 22,7% op over een periode van 13 maanden. De interventie groep daalde met 32,9%, maar de controle groep daalde oo met 20,3%.

## DISCUSSIE

Laboratorium testen worden toenemend aangevraagd in de huisartspraktijk, hoewel deze toename niet uniform verdeeld is en sommige testen minder gebruikt worden.

Richtlijnen worden beschouwd als de meest betrouwbare bron om gepast aanvraaggedrag te bepalen. Maar, richtlijnen zijn niet altijd volledig met elkaar in overeenstemming en levels of evidence worden maar zelden gegeven.

Huisartsen hebben vaak meer dan één reden om laboratorium testen aan te vragen. Zelfs met de onzekerheid over het al dan niet gepast zijn van sommige testen, kan men een belangrijke proportie van de testen als ongepast beschouwen. Aan de andere kant ontbreken aanbevolen tests vaak, waaruit blijkt dat interventies gericht moeten zijn op een kwalitatief beter aanvraaggedrag en niet alleen op het verminderen van het aantal testen.

Zoals blijkt uit de literatuur zijn interventies zoals audit en feedback, elektronische besliskundige ondersteunende systemen en financiële initiatieven mogelijk nuttig om het gedrag van artsen te beïnvloeden. Maar, deze interventies moeten goed ontworpen en georganiseerd zijn, gebaseerd op richtlijnen, ingepast in een continu proces en aangepast aan de lokale context. De kosten van dergelijke systemen kunnen kleiner zijn dan wat ze opbrengen, zoals blijkt uit onderzoek van Poley et al. waarbij de kost van de interventie 670€ per praktijk was, terwijl er per 6 maanden 847€ minder werd uitgegeven aan laboratoriumonderzoek.

# CONCLUSIES EN BELEIDSAANBEVELINGEN

- Huisartsen hebben nood aan onafhankelijke, wetenschappelijk betrouwbare en gemakkelijk toegankelijke informatie over het gepaste gebruik van laboratorium testen.
- Een nationale richtlijn over het gebruik van laboratoriumtesten in de huisartsgeneeskunde, die ook gebaseerd is op klachten en symptomen, is dringend nodig. Ook pre-analytische aspecten mogen niet vergeten worden. De wetenschappelijke huisartsen verenigingen in België zouden dit als een prioriteit moeten beschouwen. Samenwerking met klinische biologen is wenselijk.
- Integratie van deze informatie met de klinische praktijk is een absolute voorwaarde. Dit kan bereikt worden door het gebruik van herhaalde en volgehouden persoonlijke feedback, gebaseerd op de nationale richtlijn.
- Een probleem-geöriënteerd aanvraagformulier met een beperkte lijst zou het aantal ongepaste testen doen dalen. Elektronische besliskundige ondersteunende systemen kunnen dit aanvraagformulier integreren met het elektronisch medisch dossier en de nationale richtlijn.
- Bewustwording van de kosten van laboratorium testen moet verbeteren, zowel de kosten voor de ziekteverzekering als voor de patiënt. Nogmaals, elektronische besliskundige ondersteunende systemen kunnen geprogrammeerd worden om deze kosten te tonen.

# Scientific summary

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# 1 INTRODUCTION

The value of laboratory tests in general practice is widely recognised. But, their use is increasing over the last decades, and questions are asked whether this increase is justified or even possibly harmful. On the other hand, some tests might be used too little, as was shown in a previous KCE report on prenatal care, where urinary tests and hepatitis B serology were found to be underused[1].

In addition, variation between doctors in laboratory test ordering has been found to be large. Factors such as involvement in guideline development, working in a group practice and more than one year experience with a problem oriented form were found to be correlated with a lower number of lab test requests[2]. Unexplained complaints and patients' expectations have also been shown to increase the likelihood of laboratory tests being ordered[3].

Laboratory tests can be used for various purposes. One is to decrease diagnostic uncertainty in a patient presenting with a set of signs and symptoms. Another is the monitoring of a known health problem or treatment. Thirdly, a fairly large number of tests are requested for screening or case-finding purposes[4]. Finally, non medical reasons, such as patient's request, are thought to be responsible for a proportion of laboratory testing in general practice. GPs have reported personal routines; (in)tolerance of diagnostic uncertainty; time pressure; and tactical motives as reasons for test ordering[5].

Most laboratory tests are relatively cheap. But laboratory tests are typical examples of 'little ticket' technology; because they are requested in very large amounts, the total budget is quite substantial. In 1994, the Belgian Health Insurance reported laboratory tests were requested in 5-10% of all consultations, for an average cost of 10 Euro.

Next to the budgetary consequences, inappropriate testing is also potentially harmful to the patient. The more tests are performed, the higher the risk of a false positive result that induces unnecessary further testing or unnecessary treatment initiation. Especially in general practice, the risk of false positive results is fairly high, considering the low prevalence of serious illnesses in this particular setting.

The main objective of this report was to analyse the laboratory test ordering behaviour of general practitioners, and to explore interventions to influence this behaviour to more appropriate test ordering. This main objective was broken down in several research questions: What is the current situation in Belgium on the requests of laboratory tests in general practice? What are the motives of a GP to request laboratory tests? What is the optimal use of laboratory tests in general practice? Which interventions are most efficacious to change the current situation to a more optimal one?

In order to answer these questions, several analyses were performed. Firstly, the current use of laboratory tests in Belgium by GPs was analysed using administrative data. Secondly, appropriate use of laboratory tests in general was described on the basis of a literature study. Thirdly, a prospective study was set up to investigate the reasons for requesting laboratory tests in general practice. Finally, a systematic review was made on the efficacy of interventions aimed at changing laboratory test requesting behaviour.

# 2 THE USE OF LABORATORY TESTS IN BELGIUM

## 2.1 INTRODUCTION

The present chapter discusses the use of a selection of laboratory tests in Belgium. The chapter is intended to provide some background to the main topic of the guideline to laboratory tests rather than comprising an exhaustive overview.

The health care insurance in Belgium reimburses laboratory tests using a dedicated nomenclature. In this nomenclature, each item is identified by a unique number for the attribution of a fixed reimbursement amount. As a consequence, administrative data on the performance of these tests are available for analysis. The vast majority of the items are reimbursed differently when performed ambulatory rather than in hospital. The present study included ambulatory performed laboratory tests only.

Our first objective concerns the use and health care expenditure for the Belgian government of a selection of laboratory tests. We based our selection on clinical relevance of the laboratory tests for use in the general practice. Tests on urine or samples (culture, biopsy, swabs) were excluded throughout the report.

We explored the use of the selected laboratory tests in more detail for 2002 to 2004 on data retrieved from the Belgian health insurers. The following questions were studied:

1. What was the number of tests in function of the patient characteristics given the laboratory tests concerned?
2. What was the number of patients in the sample for the selected laboratory tests?
3. What is the interval of time observed between two subsequent laboratory tests for a given patient?

## 2.2 METHODOLOGY

Nomenclature numbers referring to the same test but e.g. using different means, where grouped in subclusters. The individual nomenclature numbers per subcluster can be found in the appendix to this chapter. Each subcluster was then further grouped in clusters at the level of the organ or possible pathology (see table 2.1).

**Table 2.1 Clusters and subclusters of laboratory tests**

| Cluster | Subcluster |
|---|---|
| Allergy | RAST |
| | Total IgE |
| Anemia | Iron (Fe) |
| | Fe & TIBC (total iron binding capacity) |
| | Ferritin |
| | Transferrin |
| | Vitamin B12 & folic acid |
| | Vitamin B12 |
| | Folic acid in the eryhtrocytes |
| Cardiovascular | Total cholesterol |
| | Triglycerides |
| | HDL-cholesterol |
| | LDL-cholesterol |
| Coagulation | Prothrombin time (APTT) |
| | INR/Quick |
| Blood cell count | Haemoglobin |
| | RBC & hematocrit (Hct) |
| | WBC (white blood cells, leukocytes) |
| | Platelets |
| | WBC differentiation |
| Diabetes | Glucose |
| | Glucose (≥4 determinations/ 24h) |
| | Hyperglycaemia curve |
| | Glycohemoglobin |
| | Insulin |
| | C-peptide |
| Hormonology | Follicle stimulating hormone (FSH) |
| | Luteinizing hormone (LH) |
| | Estradiol |
| | Progesterone |
| | Prolactin |
| | Testosterone |
| Inflammation | Blood sedimentation, erythrocyte sedimentation rate (ESR) |
| | C-reactive protein (CRP) |
| | Fibrinogen |
| Ions | Sodium (Na) |
| | Bicarbonate |
| | Potassium (K) |
| | Chloride (Cl) |

| | |
|---|---|
| | Calcium (Ca) |
| | Magnesium (Mg) |
| Kidney | Urea |
| | Creatinine |
| | Uric acid |
| Liver | gamma glutamyl transferase (□GT, gamma-GT) |
| | AST |
| | ALT |
| | AST & ALT |
| | LDH |
| | Alkaline phosphatase |
| | Total and direct bilirubine |
| | anti-Hepatitis A IgM (IgM anti-HAV) |
| | anti-Hepatitis A antibodies (anti-HAV) |
| | Hepatitis B s Ag (HBs Ag) |
| | Hepatitis B e Ag HBe Ag) |
| | Anti-Hepatitis B core antibodies (Anti-HBc) |
| | Anti-Hepatitis B e antibodies (Anti-HBe) |
| | Anti-Hepatitis B surface antigen (Anti-HBs) |
| | Anti Hepatitis C antibodies (anti HCV) |
| Pancreas | Amylase |
| | Lipase |
| Protein | Total protein |
| | Electrophoresis |
| Rheumatism | Rheumatoid Factor (Waaler Rose) |
| Thyroid | Thyroid Stimulating Hormone (TSH) |
| | free T4 |
| | total T4 |
| | free T3 |
| | total T3 |
| | Thyroglobulin |
| | Antimicrosomial antibodies |
| | Antithyroglobulin antibodies |
| Tumour markers[a] | CA-15-3 |
| | CEA |
| | CA-19-9 |

Data on the use of the nomenclature for the selected laboratory tests between 1995 and 2005 were extracted from the "N documents" of the National Institute for Health

[a] Prostate specific antigen (PSA) test was not considered in this study. The PSA test was studied in more detail in the KCE report 31 "Health Technology Assessment: prostate-specific-antigen (PSA) voor prostaatkankerscreening" (see HTA publications section on http://kce.fgov.be).

Care Insurance 'Rijksinstituut voor Ziekte- en Invaliditeitsverzekering (RIZIV) / Institut National d'Assurance Maladie Invalidité (INAMI)'.

Data from the RIZIV/INAMI do not allow a detailed analysis in terms of intervals between tests in the same patient. Therefore, the detailed analyses of use of the laboratory tests in 2002 to 2004 were conducted on data retrieved from the Belgian health insurers (Intermutalistisch Agentschap; IMA). IMA has drawn a sample from the total health insurers' database: 1 out of 40 (2.5%) of the Belgian population younger than 64 years and 1 out of 20 (5%) of the Belgian population over 65 (for a detailed description of the sampling procedure see [6]). Of this sample of the Belgian population, all patients with at least one of the selected laboratory tests were included. This dataset was used for the analyses in the present chapter. Data were available on number of tests, certain patient characteristics, and intervals of tests.

The following patient characteristics were considered: chronic medication use, hospitalisation status and care status. Chronic medication use was defined by the use of medication in at least one ATC class level 2 for a minimum of 90 days per year (p. 12, [7]). Hospitalisation status was defined by the presence of at least one hospital stay in the period considered for the study. Hospitalisation was categorised into three types: one day (no overnight stay), short (up to two days of hospitalisation), and long (three or more days of hospitalisation). Care status was defined by the presence of at least one stay in residential elderly care (identified by nomenclature number) or the use of home nursing (identified by type of performer of ambulatory nomenclature). An interval between two tests was defined as the number of months (=30.5 days) between the two occurrences of the test within the same patient.

Data analyses and graphs were produced using SAS 9.1.3 [8] and R 2.5.0 [9] with packages car, lattice, and MASS.

## 2.3 RESULTS

### 2.3.1 RIZIV/INAMI data on nomenclature use

With the exception of the rheumatism tests, the use of laboratory tests in all clusters increased between 1995 and 2005 (see figure 2.1). The smallest increase was about 50% for the hormonology tests while the largest increase was three times the number of tests in 1995 for the coagulation tests.

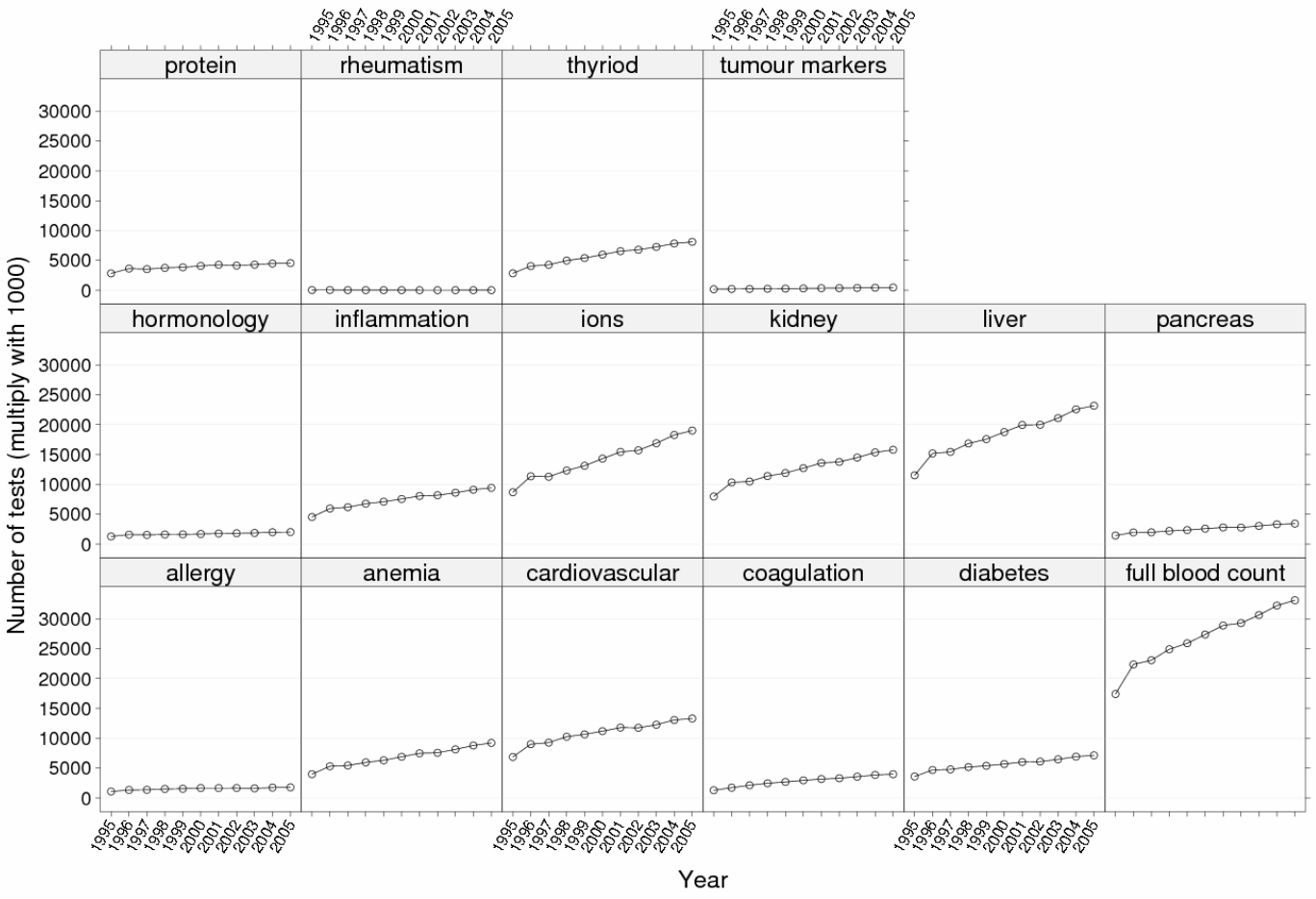



**Figure 2.1 Number of tests (thousands) per cluster in function of year.**

Subclusters within the same cluster showed a similar increase between 1995 and 2005 as their cluster. Therefore, these subclusters are not shown in detail. Exceptions were found for the anaemia, diabetes, liver, thyroid, and tumour markers tests. For the anaemia tests, all subclusters showed an increase between 1995 and 2005 except Fe & TIBC, which showed a decline in use (see figure 2.1sub1 in appendix p. 113).

For the diabetes tests, glucose (+4) and hyperglycaemia curve showed a decrease in use up until the last years. All other subclusters in this cluster showed a steady increase in use between 1995 and 2005 (see figure 2.1sub2 in appendix on p. 113).

The liver tests showed a general increase in all its subclusters with the exception of AST (see figure 2.1sub3 in appendix on p. 114).

In contrast to the other subclusters of the thyroid tests, the use of total T4 showed a decline since 1996. The use of total T3 increased until 2003 but tended to decrease since 2003 (see figure 2.1sub4 in appendix on p. 114).

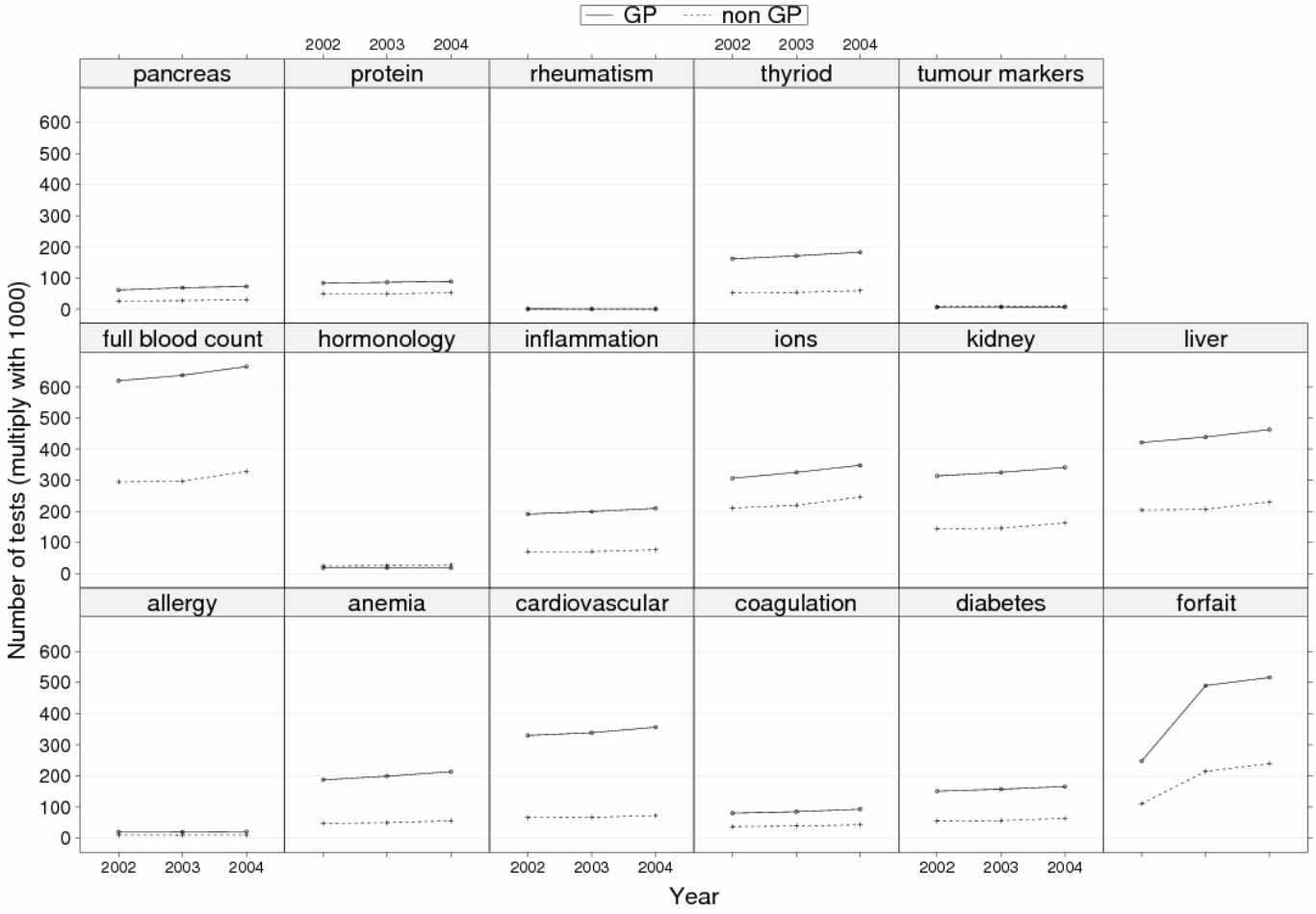
Detail of use of the selected laboratory tests on the level of the nomenclature numbers within each subcluster can be found in the appendix to this chapter.

## 2.3.2 Intermutualistisch agentschap (IMA) data

### *2.3.2.1 Numbers of laboratory tests*

More laboratory tests were ordered by general practitioners than by other specialists (see figure 2.2). Exceptions to this rule were the rheumatism, tumour markers, and hormonology tests. Similar to the RIZIV/INAMI data described previously, the use of these tests tended to increase between 2002 and 2004 with the exception of the rheumatism test.

**Figure 2.2 Number of laboratory tests (in thousands) in the IMA sample per year in function of cluster and specialism.**




The difference in the tumour marker tests between tests ordered by GPs and other specialists was largely due to CA 15.3 (see figure 2.2sub1 in appendix on p. 115). For CA 19-9 and C.E.A., the ordering behaviour was very similar for both types of ordering physician.

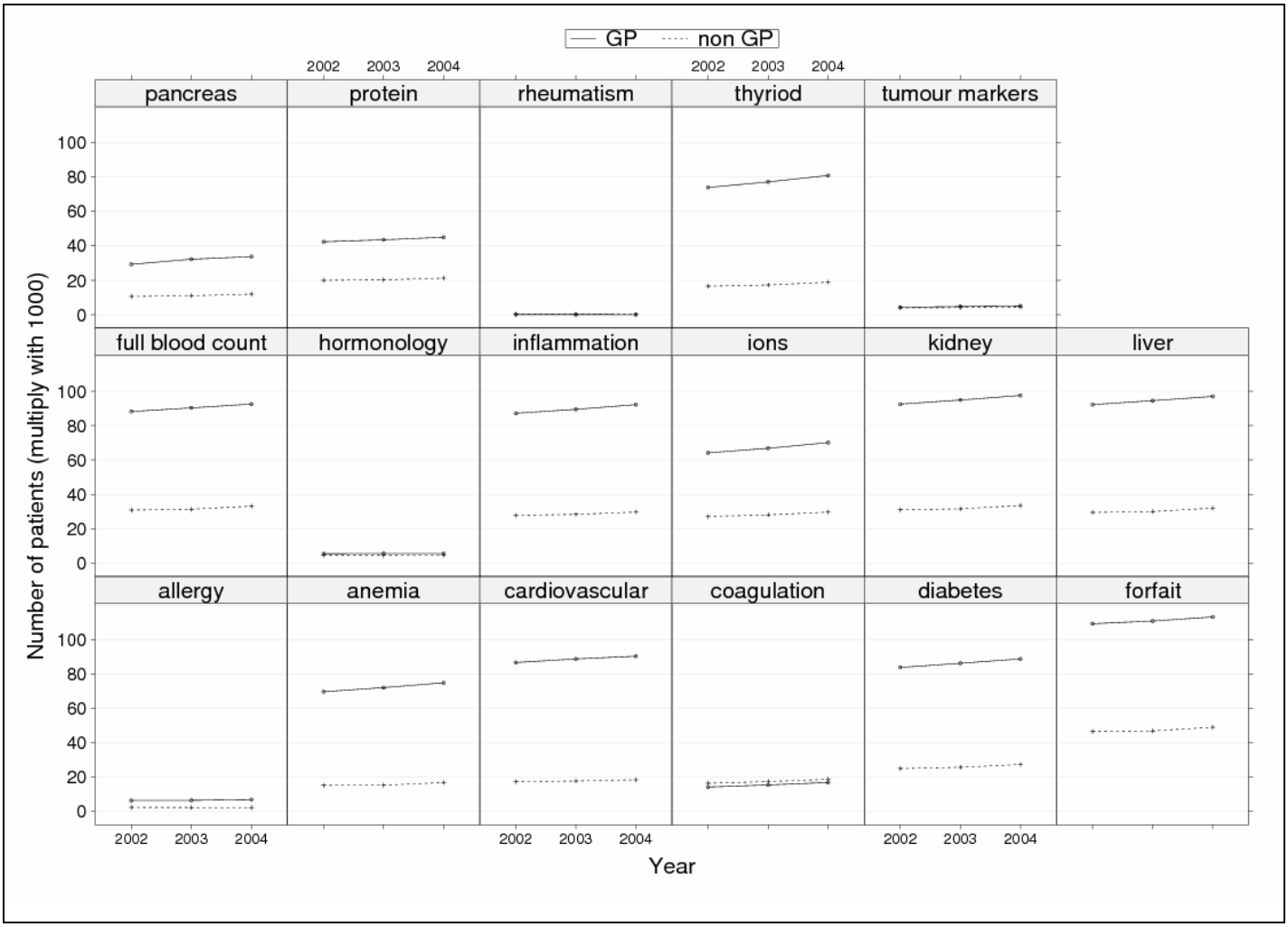
The effect of test order type in the hormonology tests was most pronounced in progesterone, LH, and estradiol (see figure 2.2sub2 in appendix on p. 115). The other subclusters showed a more moderate difference in ordering behaviour between GPs and other specialists.

For the coagulation tests, INR/Quick largely determined the larger test orders by GPs compared to other specialists (see figure 2.2sub3 in appendix on p. 116).

In general, the number of patients in the IMA sample followed the same trend as the number of tests, in other words more patients had laboratory testing; most patients

were seen by GPs in almost all clusters (see Figure 2.3. The rheumatism tests showed the reverse pattern. Although for tumour markers and hormonology tests, more tests were ordered by non GPs, less patients were seen in these clusters by non GPs than by GPs (see Figure 2.2 and 2.3). For the coagulation tests, the opposite was true: more patients were seen by non GPs compared to GPs, while the most tests were ordered by GPs.

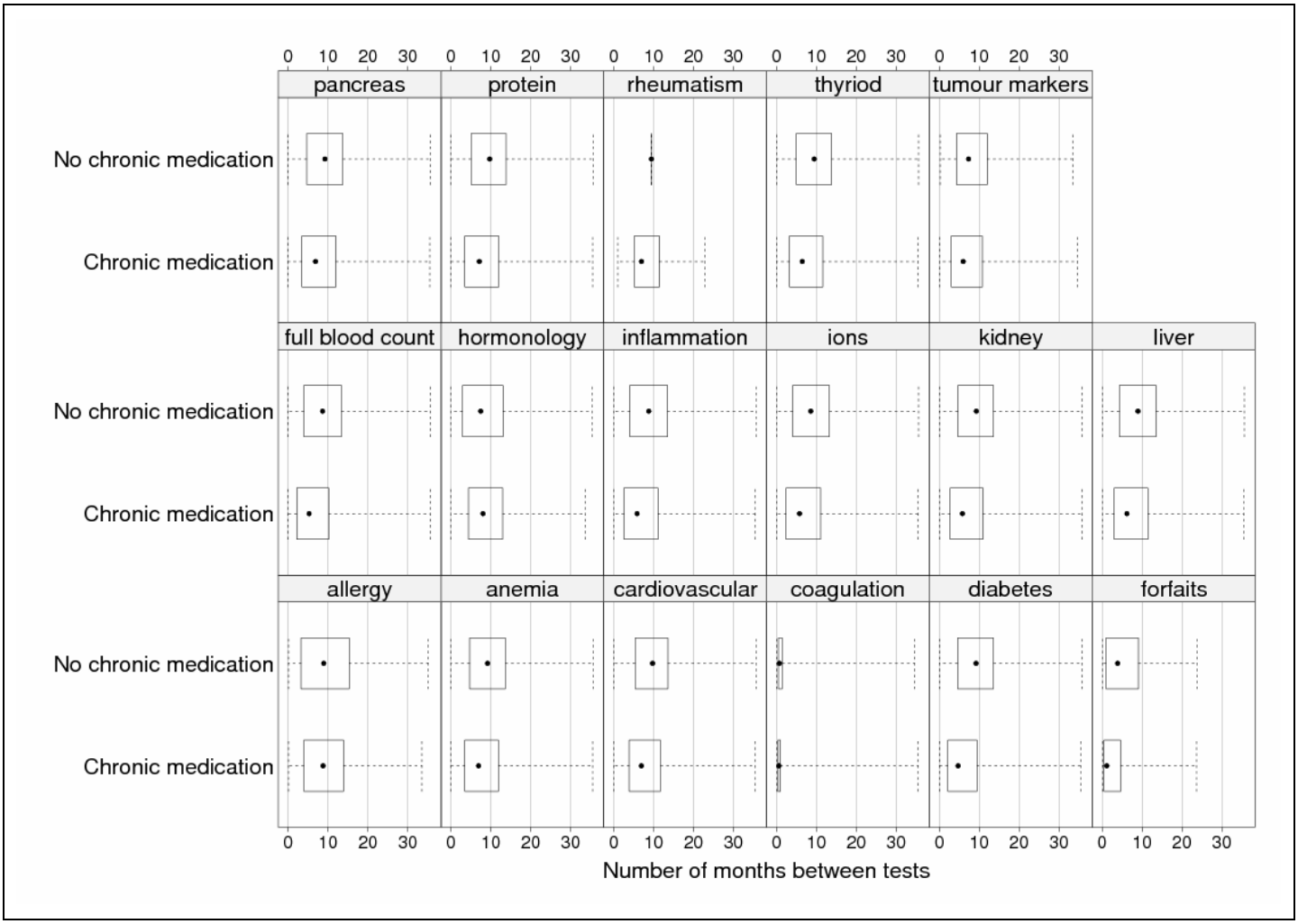
**Figure 2.3 Number of patients (in thousands) in the IMA sample per year in function of cluster and specialism.**




### 2.3.2.2 *Patient characteristics: chronic medication use*

In general, the interval of time between test orders of subsequent laboratory tests was slightly smaller for patients on chronic medication (Median=3.9 months, Q1=1.1 months, Q3=8.6 months) than for patients without chronic medication (Median=6.6 months, Q1=2.2 months, Q3=12.2 months) over all clusters (see figure 2.4). An exception were the hormonology tests which showed a slightly larger average interval time for patients on chronic medication, but did have more variability in the interval for patients without chronic medication compared to patients on chronic medication. This was largely due to progesterone, estradiol, and LH (see figure 2.4sub1 in appendix on p. 111).

**Figure 2.4 Distribution of number of months between the order of the same laboratory test per patient in the period 2002 – 2004 ordered by GP's in function of laboratory test cluster and chronic medication use**




### 2.3.2.3 *Patient characteristics: length of hospital stay*

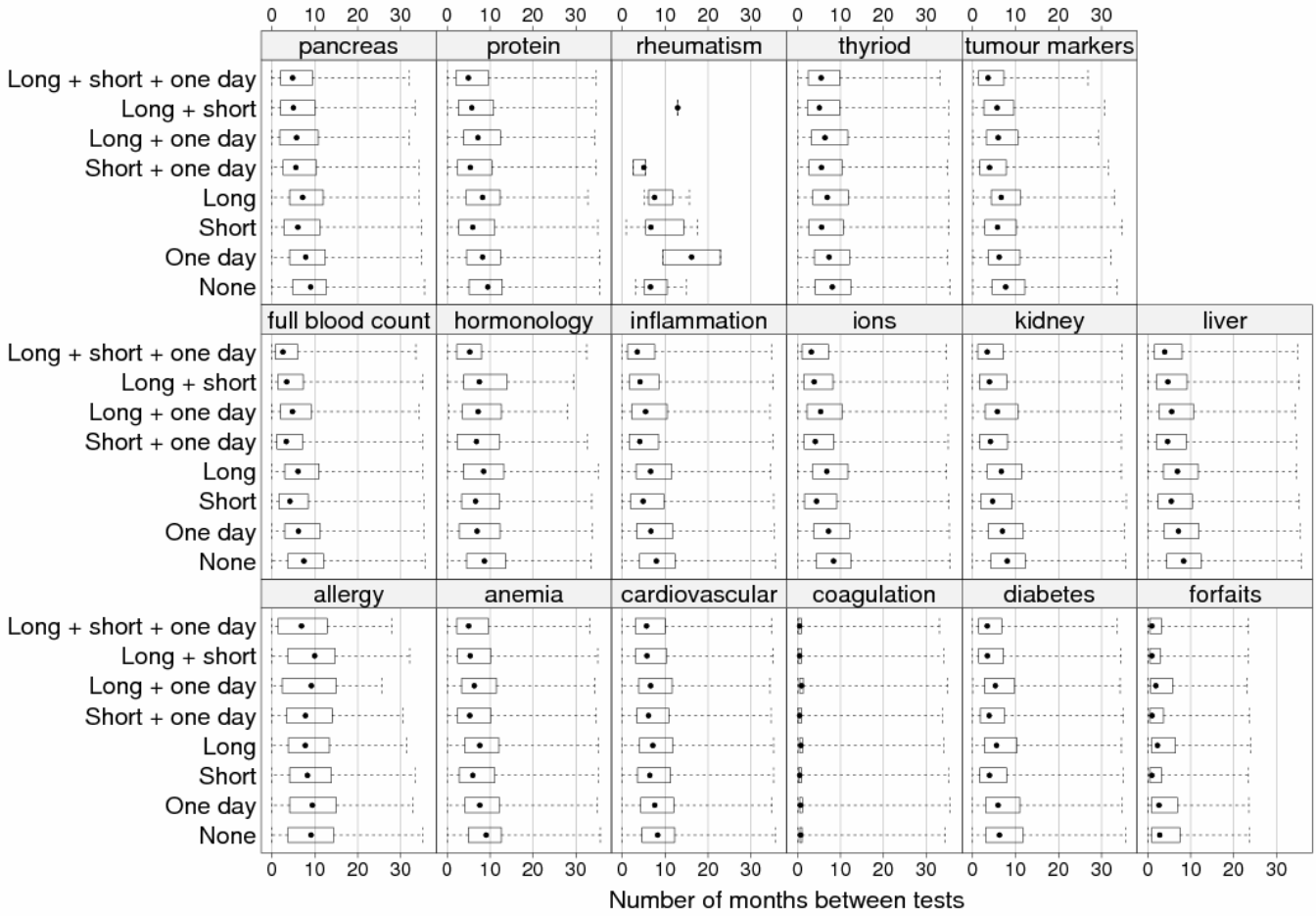
There was a general tendency for smaller intervals of time between consecutive tests for patients that had longer types of hospitalisation in the period 2002-2004 (see table 2.2 and figure 2.5).

**Table 2.2 Descriptive statistics for interval of time in months in function of length of hospital stay**

| Length of hospitalisation | Median | Q1 | Q3 |
|---|---|---|---|
| Long + short + one day | 1.3 | 0.5 | 4.1 |
| Long + short | 2.1 | 0.7 | 5.9 |
| Long + one day | 2.2 | 0.7 | 5.9 |
| Short + one day | 3.8 | 1.1 | 8.1 |
| Long | 3.3 | 1.0 | 7.6 |
| Short | 5.4 | 2.3 | 10.4 |
| One day | 5.3 | 2.1 | 10.5 |
| None | 6.7 | 3.1 | 11.9 |

Rheumatoid factor showed a clear deviation from this rule: the largest average interval was found for patients having either only one day hospitalisations or a long and short hospitalisation rather than for patients without hospitalisation.

**Figure 2.5 Distribution of number of months between the order of the same laboratory test per patient in the period 2002 – 2004 ordered by GP's in function of cluster and length of hospital stay.**



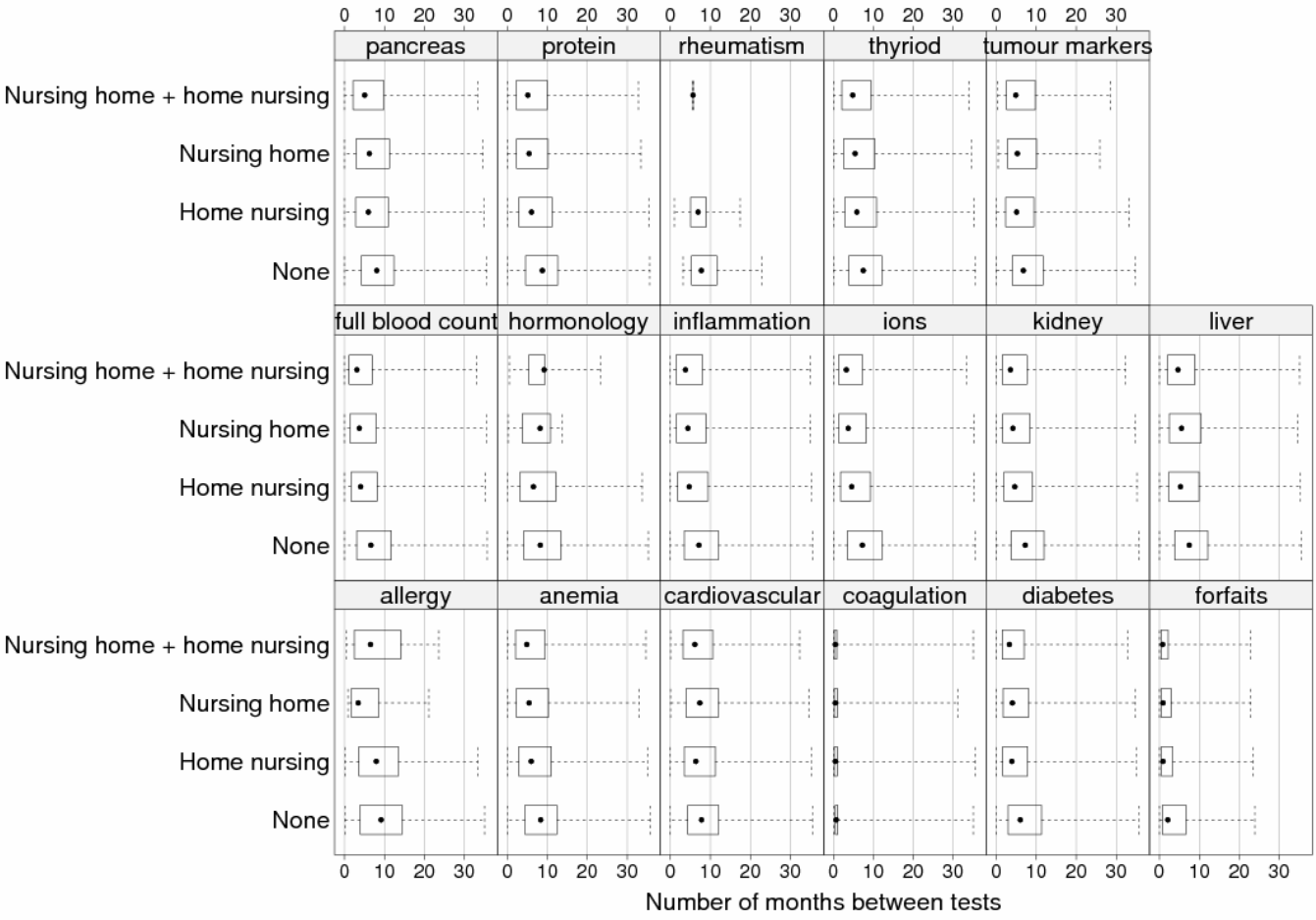

### 2.3.2.4 *Patient characteristics: care status*

In general, the time interval between consecutive tests was the smallest in patients receiving home nursing or in residential elderly care (table 2.3 and figure 2.6). Exceptions to this general tendency were the allergy, cardiovascular, and hormonology tests. The subclusters of the cardiovascular and hormonology tests showed each a similar distribution as their clusters.

**Table 2.2 Descriptive statistics for interval of time in months in function of care status**

| Care status | Median | Q1 | Q3 |
|---|---|---|---|
| Residential elderly care + home nursing | 1.9 | 0.6 | 5.6 |
| Residential elderly care | 2.8 | 0.9 | 7.1 |
| Home nursing | 2.8 | 0.9 | 6.8 |
| None | 5.5 | 2.1 | 11.0 |

**Figure 2.6 Distribution of number of months between the order of the same laboratory test per patient in the period 2002 – 2004 ordered by GP's in function of cluster and care status.**




The interval between laboratory tests in patients both receiving home nursing and in residential elderly care was much larger for RAST tests compared to patients in the other care categories (see figure 2.6sub1 in appendix on p. 117).

### *Keypoints*

- **RIZIV/INAMI data showed an increase of use of the selected laboratory tests in the last 10 years. The extent of this increase depended on cluster: e.g. 1.5 times for the full blood count tests and three times for the coagulation tests. Part of this increase can be explained by an increase in patients as shown by the IMA data.**
- **Over all tests in the period 2002-2004, patients with chronic medication received on average the same tests within an interval of about 4 months or about thrice a year. For patients without chronic medication, this was about every 7 months. However a large variation existed between patients and tests.**
- **Having had a (longer) hospitalisation, or a residential elderly care stay or home nursing tended to be related to smaller intervals of time between consecutive tests for most test groups.**

# 3 APPROPRIATE USE OF LABORATORY TESTS IN GENERAL PRACTICE

## 3.1 INTRODUCTION

It has been suggested that inappropriate test ordering is one of the reasons for the increased laboratory use. One of the possible explanations of inappropriate test ordering is fear of missing a serious illness, fear of litigation, the availability of an increasing range of diagnostic tests, and lack of knowledge on the utility of tests. In addition to contributing to exaggerated costs, inappropriate testing can also be harmful to the patient[10]. The probability of false positive results increases, leading to unnecessary concern and additional testing or initiating inappropriate treatment[11].

Several studies were performed to positively influence the use of laboratory tests. Although some studies aimed at simply reducing the number of tests requested, others tried to modify physician behaviour to use laboratory tests more appropriately. However, in order to do this, appropriate and inappropriate test ordering ought to be described. Several definitions of both have been used over the years. Van Walraven et al. described implicit and explicit criteria to define inappropriate laboratory testing, such as whether the test result was abnormal or changed therapy[12].

In this review, criteria for appropriate use of laboratory tests in primary care are summarized.

## 3.2 METHODS

The literature was searched in the two main medical databases: Medline and Embase (1966-September 2006).

The search terms combined terms on laboratory test utilization and primary care.

Search string for Medline:

("Family Practice"[MeSH] OR "Physicians, Family"[MeSH] OR general pract* OR GP) AND ("Laboratory Techniques and Procedures/economics"[MeSH] OR "Laboratory Techniques and Procedures/statistics and numerical data"[MeSH] OR "Laboratory Techniques and Procedures/trends"[MeSH] OR "Laboratory Techniques and Procedures/utilization"[MeSH])

Search string for Embase:

('utilization review'/exp OR utilization AND 'review'/exp OR 'physician'/exp AND practice AND pattern OR diagnostic AND test AND utilization OR appropriate AND use) AND ('general practice'/exp OR 'family'/exp AND practice OR 'family'/exp AND 'physician'/exp OR primary AND care) AND ('blood examination'/exp OR 'clinical laboratory'/exp) AND [embase]/lim AND [1966-2006]/py)

Systematic reviews were searched first, using Clinical Queries in PubMed. Subsequently, original articles were searched. In addition, the reference lists of the selected articles were searched for any missing relevant publications.

All articles were subsequently selected based on title and abstract according to the following selection criteria:

Inclusion criteria:

- Laboratory tests
- Family practice
- Utilization / appropriate use

Exclusion criteria

- Screening tests or strategies

- Pathology tests
- Imaging
- Narrative review, editorial, letter without research results

No language restrictions were applied. Studies reporting on interventions to influence laboratory testing or studies reporting a utilization review were eligible provided they reported appropriateness criteria in their methods section.

A formal quality appraisal was not performed on the articles selected, as it was the goal of the review to simply describe what criteria have been used to define appropriate use.

All relevant information was extracted from the studies and summarized in evidence tables.

## 3.3 RESULTS

Searching for systematic reviews, 8 articles were found. The literature search on original studies identified 317 articles, discarding duplicates.

Applying selection criteria, no systematic review was selected for further review. From the original studies, 23 were initially selected for further review on full text. After evaluation for eligibility according to the in and exclusion criteria, nine articles were finally selected for inclusion in the review[13-21]. Evidence tables are in appendix (table 3.1)

All studies were performed in primary care, being general practice in most cases (n=8) and one outpatient clinic of an academic centre[13]. Not all articles mentioned the number of physicians or patients involved in the various studies. Number of physicians ranged from 40 to 85; number of patients from 500 to an entire NHS Trust serving approximately 500.000 persons.

Tests that were included in the studies ranged from all possible tests that were requested by the participating physicians, to one specific set of tests relating to one specific health problem, e.g. thyroid testing.

Two articles specifically stated expert opinion to be the criterion of appropriateness[14 15]. In Larson's study, GPs were offered an educational session in which one professor explained what appropriate laboratory test utilization was. In the other study, a panel of academics served as a benchmark of good clinical practice. Neither study stipulated on what these academics based their opinion.

Four articles based their criteria for appropriateness on guidelines that were published previously, three of which were the guidelines developed by the Dutch College of General Practice[13 16 17 21].

From the remaining three articles, one article defined an appropriate testing strategy for suspected thyroid disorder, as an initial screen using TSH, followed by other thyroid tests if TSH was abnormal[18]. The justification for this criterion was not given.

Zaat et al. stated that according to the literature on sensitivity and specificity of laboratory tests, only 15 tests were useful in a low prevalence population, such as general practice[20]. The authors reference to the first author's doctoral thesis as the source of this selection.

Finally, Bailey et al. found some tests to be more appropriate for hospital use rather than use in general practice, without however referring to the criteria with which this appropriateness was determined[19].

## 3.4 DISCUSSION

In this review, a limited number of studies were retrieved, in which appropriateness criteria for laboratory test utilisation were described.

Most studies used guidelines as the criterion for appropriateness. Provided these guidelines were developed in a methodologically sound and valid fashion, they could indeed be a good basis. Reasons for testing are linked to possible consequences on therapy or prognosis. In the Netherlands, a nationwide agreement on laboratory testing

in primary care has equally been based on guidelines, and in those cases where guidelines were not available, a literature search on that specific subject was made (http://nhg.artsennet.nl/).

Two studies used expert opinion, to judge whether tests were appropriate or not. But, it is not stated whereupon this expert opinion was based. In addition, the reader is unable to evaluate whether these experts were up to date with the literature or clinical decision making at the time of the study.

Explicit criteria of appropriateness are dependent on the specific test and the indication for which it is used. For example, in one study, the TSH was proposed as an initial screen for thyroid disorders, reserving the other tests for those patients with an abnormal TSH result. This approach is supported by several studies, in which TSH was found to be a sensitive test for thyroid disorders[22 23] and has been shown to be cost-effective[24]. Similarly, one study considered only those tests appropriate with a sensitivity/specificity profile that suits a low prevalence population such as general practice.

Van Walraven et al. identified studies in which an abnormal test result was considered a criterion for appropriateness, or a change in patient management[12]. In our review, neither study used these criteria. To our opinion, considering only those tests with an abnormal test result as appropriate is not valid. If all tests with a normal test result are inappropriate, performing tests for the exclusion of a disease would be inappropriate. This is, certainly in a low prevalence setting such as general practice, not a valid assumption. In general practice, an important task is exactly to exclude a number of diseases. In addition, considering only those tests to be appropriate that have led to a change in management, would exclude any testing for prognostic purposes, reassurance of the patient and excluding disease. Equally, this assumption is not valid.

Essentially, most studies used diagnostic evidence as the basis for deciding on appropriateness, whether or not this evidence was summarized in guidelines. It has been shown that test characteristics can change according to the setting in which they are applied. This is particularly important for general practice, as many diagnostic tests are evaluated in selected populations with a high prevalence of disease, whereas general practice serves by definition an unselected population with a low prevalence of disease. Setting-specific evidence of a test's diagnostic efficacy is important in deciding on the usefulness of the test. In addition, a test may be used in various indications, for example as a triage test at the beginning of the clinical pathway, or at the end of a clinical pathway to rule in a certain disease. In the former case, the test should have maximum sensitivity. In the latter case, the test should have maximum specificity.

### *Key points*

- **Appropriateness is mostly based on guidelines**
- **Explicit criteria for all laboratory tests in general are not definable**
- **Tests are appropriate when there is setting-specific evidence proving they have test characteristics suitable for the goal of the test.**

# 4 SYNTHESIS OF EXISTING GUIDELINES

## 4.1 INTRODUCTION

It was shown in the previous chapters that guidelines are the most cited source of information when it comes to assessing appropriate test ordering behaviour. Many institutions and professional organisations have set up a guideline development programme, to establish guidelines on clinically relevant topics. For general practitioners, guidelines can offer guidance on which tests ought to be requested in which situation.

In this chapter, we aimed to summarise recommendations on laboratory tests from existing guidelines. It was by no means the intention to construct a guideline and offer clinical recommendations to GPs on how to use laboratory tests. By consequence, the recommendations that are summarised should not be used as such. This synthesis was mainly meant as input for the next chapter on appropriate test ordering behaviour.

## 4.2 METHODS

Databases were selected that are publicly available and develop guidelines for primary care or multidisciplinary guidelines: NHG standaarden, WVVH richtlijnen, SIGN, New Zealand Guidelines Group and Prodigy. All the guidelines listed on the developers' website were hand searched.

The selection criteria were: the guideline should be relevant to primary care and include a reference to laboratory testing, being a recommendation in favour or against a test.

All information on laboratory testing was subsequently extracted from the guidelines and summarised in an Excel sheet. As in the whole of the report, urine based testing or cultures were not considered. Data included the target condition in which the indication for testing was found, the guideline developer and whether or not levels of evidence or grades of recommendations were used to sustain the indication. The indications for laboratory testing were then assigned to an ICPC code, and to an indication-class, being case-finding, diagnosis, follow-up, therapeutic drug monitoring or therapeutic drug initiation.

## 4.3 RESULTS

Searching the different databases, 118 guidelines were found. A list of all guidelines is available from the authors on request. Only one guideline referred specifically to laboratory testing in primary care, developed by the NHG in collaboration with the National College of Clinical Chemists and the Collaboration of Laboratories (further referred to as the SAN guideline). Most guidelines were developed for a disease or syndrome and contained only one or a few paragraphs on laboratory tests.

In total, 207 indications for laboratory testing were found in the 118 guidelines. Four indications related to case finding, 150 indications were diagnostic, 26 were for follow-up of the target condition, 17 were on therapeutic drug monitoring and 10 were on the initiation of a therapeutic drug.

The 207 indications referred to 88 different ICPC codes. The most frequent codes were those for diabetes, insulin and non-insulin dependent (n=20), rheumatoid arthritis (n=12) and hypertension (n=11).

Levels of evidence or grades of recommendation were used in only 24 indications. All other indications did not have any reference to the levels of evidence that underlied the recommendation or the grade of recommendation that could be assigned to it.

Totalling all tests for all indications, 709 recommendations in favour of a laboratory test were made. The test with the highest number of recommendations was haemoglobin, which was recommended 54 times, on 35 different indications (some indications were mentioned in more than one guideline). Haemoglobin was followed by creatinine, which

was recommended 53 times for 22 different indications. Glucose took third place with 49 recommendations for 18 different indications.

Some tests commonly used in Belgian health care were not recommended in any of the guidelines: Chloride, magnesium, bicarbonate, amylase and lipase, fibrinogen, CMV IgM and IgG, total IgE and HBs antibodies. It should be noted, however, that no guidelines were identified on pancreatitis, explaining the absence of any recommendation on amylase and lipase.

For each indication, the number of laboratory tests recommended ranged from 0 to 13. The median was 2, and the average 3.3 tests per indication.

## 4.4 RECOMMENDATIONS PER INDICATION

### 4.4.1 Hyperhidrosis, ICPC code A09

One guideline was available, from Prodigy. Levels of evidence or grades of recommendation were not provided.

For generalised hyperhidrosis, recommended lab tests are:

- Hb
- RBC + Hct
- WBC
- Platelets
- Glucose
- AST+ALT
- CRP
- Urea
- K
- Na
- TSH
- ESR

For focal hyperhidrosis, lab tests are not recommended.

### 4.4.2 Suspicion of infectious mononucleosis, ICPC code A75

Two guidelines were available, from the NHG and NHG-SAN. Levels of evidence or grades of recommendation were not provided.

Lab tests recommended:

| | NHG | SAN |
|---|---|---|
| • WBC | | √ |
| • WBC differentiation | √ | |
| • EBV IgM | √ | √ |
| • EBV IgG | √ | √ |

### 4.4.3 Adverse effect of a therapeutic drug

#### *4.4.3.1 Myelotoxic drugs, ICPC code A85*

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation provided.

Lab tests recommended:

- Hb
- RBC + Hct
- WBC
- WBC differentiation
- Platelets

#### *4.4.3.2 Hepatotoxic drugs, ICPC code A85*

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation provided.

Lab tests recommended:

- AST+ ALT

#### *4.4.3.3 Nephrotoxic drugs, ICPC code A85*

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation provided.

Lab tests recommended:

- Creatinine

### 4.4.4 Hypersensitivity, ICPC code A92

One guideline was available, by NHG (SAN). No levels of evidence or grades of recommendation provided.

Lab tests recommended:

- RAST, in case of diagnostic uncertainty after history taking, and in case of a serious allergic reaction in a neonate or serious eczema in children between 9 months and 2 years of age.

### 4.4.5 General check-up/vague complaints, ICPC code A98

One guideline was available by NHG-SAN. No levels of evidence or grades of recommendation provided.

The authors stress the importance of ordering as little tests as possible, as the risk of false positive results is fairly high in asymptomatic patients. In addition, the ESR is only recommended in patients presenting with symptoms. In asymptomatic persons, ESR is of little or no value.

Lab tests recommended:

- Hb
- Glucose
- ALT
- ESR
- Creatinine
- TSH

### 4.4.6 Statin therapy, ICPC code B34

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation provided.

Lab tests recommended before start of therapy:

- AST + ALT
- CK

Tests recommended on deciding whether to start statin therapy at all relate to the cardiovascular risk assessment, and included total cholesterol and HDL cholesterol.

### 4.4.7 Heparin therapy, ICPC code B34

One guideline was available, by SIGN. No levels of evidence or grades of recommendation provided.

Difference is made on therapy initiation and therapy monitoring.

Before starting therapy, SIGN recommends the following lab tests:

- Hb
- RBC + Hct
- WBC
- Platelets
- PT/INR
- APTT
- AST + ALT
- Creatinine
- K
- Na

Therapy monitoring is done using

- APTT

### 4.4.8 Oral anticoagulant therapy, ICPC code B34

Three guidelines were available, by NHG-SAN, SIGN and Prodigy. No levels of evidence or grades of recommendation provided.

As with heparin therapy, SIGN recommends the same tests before starting treatment with oral anticoagulants.

For therapeutic drug monitoring, lab test recommended by all 3 guidelines is:

- PT/INR

### 4.4.9 Haemochromatosis, ICPC code A79

One guideline was available, by NHG-SAN. No levels of evidence or grades of recommendation were provided.

Lab tests recommended are:

- Transferrin saturation measurement as a first step

In case of an abnormal result:

- Hb
- RBC + Hct
- Reticulocytes
- Glucose

- ALT
- ESR (or CRP)
- Ferritin

### 4.4.10 Anaemia, ICPC code B80

Four guidelines were available, one by NHG-SAN, one by NHG and two by Prodigy. No levels of evidence or grades of recommendation provided.

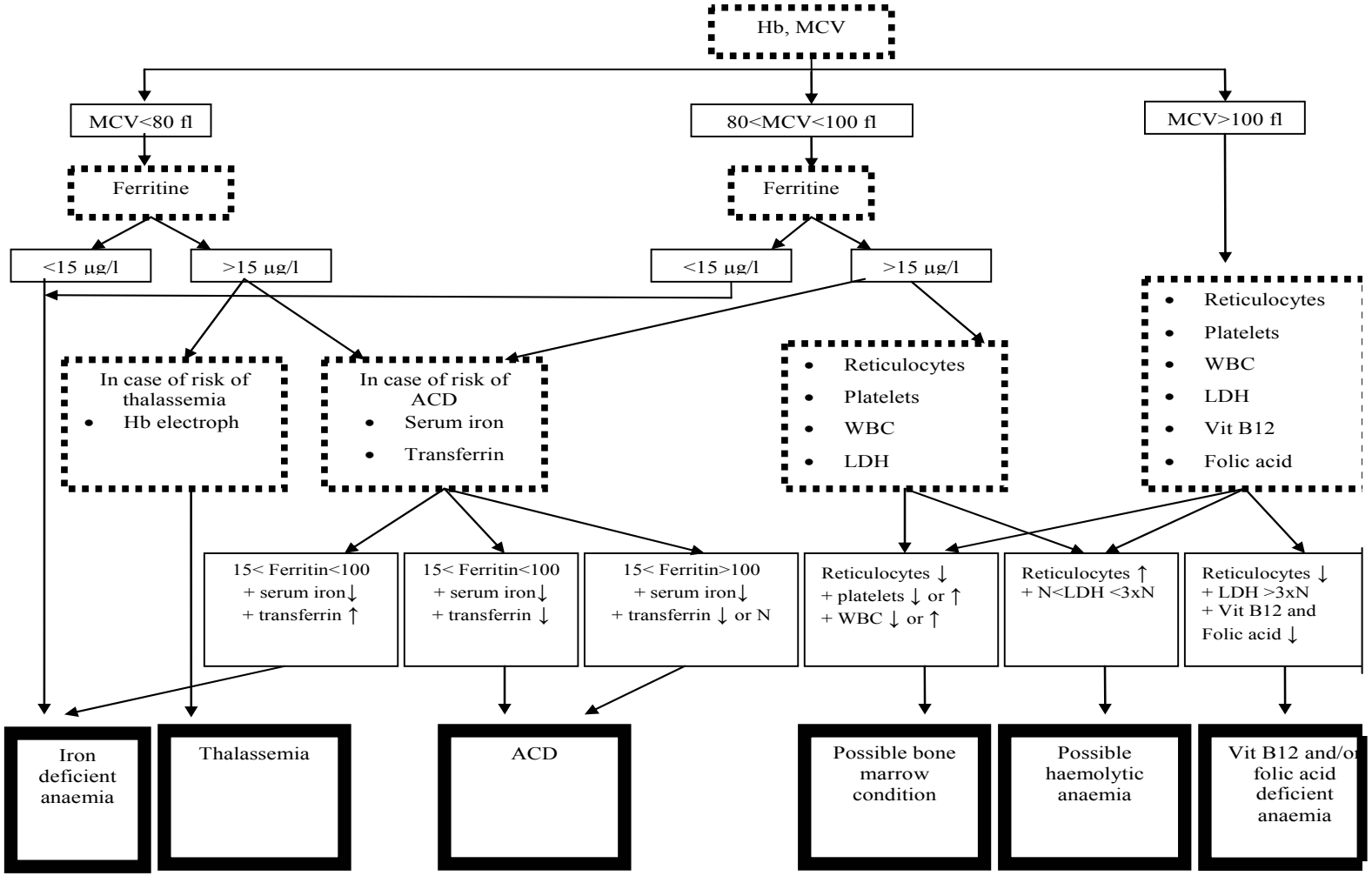
The algorithm below summarises the recommendations.

Abbreviations used:

ACD = anaemia by chronic condition

After treatment has been established for anaemia, treatment success is evaluated using:

- Hb


Hb, MCV
MCV<80 fl
80<MCV<100 fl
MCV>100 fl
Ferritine
Ferritine
<15 µg/l
>15 µg/l
<15 µg/l
>15 µg/l
In case of risk of thalassemia
Hb electroph
In case of risk of ACD
Serum iron
Transferrin
Reticulocytes
Platelets
WBC
LDH
Reticulocytes
Platelets
WBC
LDH
Vit B12
Folic acid
15< Ferritin<100 + serum iron↓ + transferrin ↑
15< Ferritin<100 + serum iron↓ + transferrin ↓
15< Ferritin>100 + serum iron↓ + transferrin ↓ or N
Reticulocytes ↓ + platelets ↓ or ↑ + WBC ↓ or ↑
Reticulocytes ↑ + N<LDH <3xN
Reticulocytes ↓ + LDH >3xN + Vit B12 and Folic acid ↓
Iron deficient anaemia
Thalassemia
ACD
Possible bone marrow condition
Possible haemolytic anaemia
Vit B12 and/or folic acid deficient anaemia

### 4.4.11 Increased bleeding tendency, ICPC code B83

One guideline was available, by NHG-SAN. No levels of evidence or grades of recommendation provided.

The following lab tests are recommended:

- Platelets
- PT/INR
- APTT

### 4.4.12 HIV infection, ICPC code B90

One guideline was available, by NHG (SAN). No levels of evidence or grades of recommendation provided.

In patients with suspicion of HIV infection, the following lab test is recommended:

- HIV antibodies

### 4.4.13 Diarrhoea, ICPC code D11

One guideline was available, by NHG (SAN). No levels of evidence or grades of recommendation provided.

No laboratory tests are recommended.

### 4.4.14 Neonatal jaundice, ICPC code D13

One guideline was available, by NHG (SAN). No levels of evidence or grades of recommendation provided.

Lab test recommended:

- Bilirubin

### 4.4.15 Aphtous ulcer, ICPC code D83

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation provided.

Lab tests recommended in case of a suspicion of systemic disease, malabsorption or nutritional deficiency (recurrent episodes):

- Hb
- RBC + Hct
- Ferritin
- Vit B12
- Folic acid in serum and red cells

### 4.4.16 Hiccups, ICPC code D29

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation provided.

Lab tests recommended in case of persisting hiccups lasting more than 24 hours or frequent recurrence:

- Hb
- RBC + Hct
- Glucose

- AST + ALT
- ESR
- Creatinine
- Urea
- K
- Na
- Ca

### 4.4.17 Liver disease, ICPC code D97

Two guidelines were available, by NHG and NHG-SAN. No levels of evidence or grades of recommendation provided.

Lab tests recommended in patients suspected of any liver disease:

- Gamma-GT
- AST+ALT

#### *4.4.17.1 Hepatitis A, ICPC code D72*

One guideline was available, by NHG-SAN. No levels of evidence or grades of recommendation provided.

Lab test recommended in patients with evidence of liver disease and suspected of hepatitis A:

- IgM HAV

#### *4.4.17.2 Hepatitis B, ICPC code D72*

One guideline was available, by NHG-SAN. No levels of evidence or grades of recommendation provided.

Lab test recommended in patients with evidence of liver disease and suspected of hepatitis B:

- HBs Ag
- HBc IgM

#### *4.4.17.3 Hepatitis C, ICPC code D72*

Two guidelines were available, by NHG-SAN and SIGN. SIGN provided levels of evidence or grades of recommendation.

Lab test recommended in patients with evidence of liver disease and suspected of hepatitis C:

- HC Ab
- HCV-RNA in case of a positive test on antibodies (use a sensitive enough assay to detect 50-100IU/ml to detect current infection)

SIGN grades the recommendation as 'B': based on good clinical studies, but no randomised clinical trials.

### 4.4.18 Gastro-oesophageal disease, dyspepsia, ICPC code 84

One guideline was available, by Prodigy. Levels of evidence or grades of recommendation are provided.

Lab tests recommended in new patients in order to detect any alarm symptoms:

- Hb
- RBC + Hct

Grade of recommendation 'D': expert opinion.

### 4.4.19 Diverticular disease and diverticulitis, ICPC code D92

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation provided.

Lab tests recommended in patients suspected of diverticulitis:

- Hb
- RBC + Hct
- WBC

### 4.4.20 Irritable bowel syndrome, ICPC code D93

One guideline was available, by NHG. No levels of evidence or grades of recommendation provided.

Lab tests are routinely not recommended. In selected patients in whom diagnostic uncertainty remains for a possible inflammatory bowel disease malignancy or treatment failure, the following tests are recommended:

- Hb
- RBC + Hct
- WBC

### 4.4.21 Coeliac disease, ICPC code D94

One guideline was available, by NHG-SAN. No levels of evidence or grades of recommendation are provided.

Lab test recommended in these patients:

- Human tissue transglutaminase

### 4.4.22 Cardiovascular risk calculation, ICPC code K22

Four guidelines were available, by Prodigy, NHG, New Zealand guidelines group and SIGN. The last two provided grades of recommendation.

Lab tests recommended calculating cardiovascular risk:

| | Prodigy | NHG | NZGG | SIGN |
|---|---|---|---|---|
| Glucose | √ | √ | √ | √ |
| Total chol | √ | √ | √ | √ |
| Triglyc | √ | √ | √ | |
| HDL chol | √ | √ | √ | √ |
| Tot chol/HDL | √ | √ | | |
| LDL | √ | √ | √ | √ |

SIGN grades the recommendation as 'B', and NZGG as 'C'.

### 4.4.23 Angina pectoris, ICPC code K74

Three guidelines were available, by Prodigy, SIGN and NHG-SAN. Grades of recommendation were provided by Prodigy.

Tests recommended in patients with stable angina pectoris:

| | Prodigy | SAN | SIGN |
|---|---|---|---|
| Hb | √ | √ | √ |
| Glucose | √ | | √ |
| Tot chol | √ | | √ |
| Triglyc | √ | | √ |
| HDL | √ | | √ |
| TSH | √ | √ | |

Prodigy grades the recommendation on lipid testing as 'C' and on Hb and glucose as 'GPP' (=good practice point; based on clinical experience of the guideline development group).

### 4.4.24 Acute coronary syndrome, ICPC code K74-75

Two guidelines were available, by NHG and NHG-SAN. No levels of evidence or grades of recommendation were provided.

Lab tests recommended by SAN in a selected group of patients (complaints started >24 hours to 5 days ago, and have disappeared since):

- CK
- Troponin T or I

For the follow-up of patients after myocardial infarction, the following tests are recommended by NHG:

- Glucose
- Creatinine
- K
- Tot chol
- Triglycerides
- HDL

### 4.4.25 Heart failure, ICPC code K77

Three guidelines were available, by Prodigy, NHG-SAN and SIGN. Only the last guideline provided grades of recommendation.

Lab tests recommended in the diagnostic phase of heart failure:

| | Prodigy | SAN | SIGN |
|---|---|---|---|
| Hb | √ | √ | √ |
| RBC + Hct | √ | √ | √ |
| WBC | | | √ |
| Glucose | √ | √ | √ |
| Gamma-GT | | | √ |
| AST+ALT | √ | | √ |
| AF | | | √ |
| Creatinine | √ | | √ |
| Urea | √ | | √ |
| K | √ | | √ |
| Na | √ | | √ |
| Tot chol | √ | | √ |
| Triglyc | √ | | |
| HDL | √ | | |
| TSH | √ | √ | √ |
| BNP | √ | √ | |

SIGN grades the recommendation as 'C'.

Before and during diuretics or ACE inhibitor treatment, lab tests are recommended:

| | Prodigy | SAN |
|---|---|---|
| Creatinine | √ | √ |
| Urea | √ | |
| K | √ | √ |
| Na | √ | √ |

### 4.4.26 Atrial fibrillation, ICPC code K78

Three guidelines were available, by Prodigy, NHG-SAN and NZGG. No levels of evidence or grades of recommendation were provided.

Lab tests recommended at the diagnosis of atrial fibrillation:

| | Prodigy | SAN | NZGG |
|---|---|---|---|
| Hb | √ | √ | |
| RBC + Hct | √ | | |
| PT/INR | | | √ |
| Glucose | | √ | |
| Creatinine | √ | | √ |
| K | √ | | |
| Na | √ | | |
| TSH | √ | √ | √ |

In case anticoagulation is planned, Prodigy recommends the following tests:

- PT/INR
- APTT
- AST+ALT

Both NHG-SAN and Prodigy recommend the following tests in case digoxin treatment is planned and annually thereafter during treatment:

- Creatinine
- K

### 4.4.27 Hypertension, ICPC code K86

Four guidelines were available, by Prodigy, NHG-SAN, WVVH and SIGN. The latter two provided grades of recommendation. The SIGN guideline is specifically directed at older adults.

Lab tests recommended at the diagnosis of hypertension:

| | Prodigy | SAN | WVVH | SIGN |
|---|---|---|---|---|
| Hb | | | √ | √ |
| RBC+Hct | | | √ | √ |
| Glucose | √ | √ | √ | √ |
| Gamma-GT | | | | √ |
| Creatinine | √ | √ | √ | √ |
| Uric acid | | | √ | √ |
| K | √ | √ | √ | √ |
| Ca | | | | √ |
| Tot chol | √ | √ | √ | √ |
| Triglyc | | | | √ |
| HDL | √ | √ | | √ |
| TSH | | | | √ |

SIGN recommends Gamma-GT to detect alcohol abuse, and Ca to exclude hyperparathyroidism. They give a grade C recommendation to the recommendation of a cardiovascular risk assessment in all hypertensive patients.

WVVH grades their recommendations as level 1.

Prodigy recommends the following tests in the follow-up of hypertensive patients:

- Creatinine
- K

Before starting ACE inhibitors, after 2 weeks of treatment and annually thereafter, Prodigy recommends:

- Urea
- Estimated glomerular filtration rate
- K
- Na

According to SAN and Prodigy, before starting diuretics:

- K

### 4.4.28 Transient ischemic attack, ICPC code K89

Two guidelines are available, by Prodigy and NHG-SAN. No levels of evidence or grades of recommendation are provided.

The following tests are recommended when a patient is diagnosed with a TIA, in case these were not already performed in the stroke unit:

| | Prodigy | SAN |
|---|---|---|
| Hb | √ | |
| RBC+Hct | √ | |
| WBC | √ | |
| Platelets | √ | |
| PT/INR | √ | |
| Glucose | √ | √ |
| ESR | √ | √ |
| Tot chol | √ | √ |
| HDL | √ | √ |

### 4.4.29 Pulmonary embolism, ICPC code K93

One guideline was available, by SIGN. Levels of evidence or grades of recommendation were not provided.

No lab tests are recommended to diagnose pulmonary embolism.

### 4.4.30 Deep venous thrombosis, ICPC code K94

Three guidelines were available, by Prodigy, NHG-SAN and SIGN. Levels of evidence or grades of recommendation were not provided.

Lab tests recommended for the diagnosis of DVT:

| | Prodigy | SAN | SIGN |
|---|---|---|---|
| • D-dimer | √ | | √ |

### 4.4.31 Thrombophlebitis, ICPC code K94

One guideline was available, by Prodigy. Levels of evidence or grades of recommendation were not provided.

No lab tests are recommended in the diagnosis or the management of thrombophlebitis.

### 4.4.32 Rheumatoid arthritis, ICPC code L88

#### *4.4.32.1 Rheumatoid arthritis*

Three guidelines were available, by Prodigy, NHG-SAN and SIGN. Levels of evidence or grades of recommendation were not provided.

Lab tests recommended for the diagnosis of rheumatoid arthritis:

| | Prodigy | SAN | SIGN |
|---|---|---|---|
| Hb | √ | | √ |
| RBC+Hct | √ | | √ |
| WBC | √ | | √ |
| Platelets | √ | | √ |
| Gamma-GT | √ | | √ |
| ALT+AST | √ | | √ |
| AP | √ | | √ |
| CRP | √ | | √ |
| ESR | √ | | √ |
| Urea | | | √ |
| K | | | √ |
| RF | √ | √ | √ |
| ANA | √ | √ | √ |

For patients experiencing a flare-up, Prodigy recommends:

- CRP
- ESR

For the follow-up of patients diagnosed with RA, SAN recommends:

- Hb
- RBC+Hct
- ESR

#### *4.4.32.2 Polymyalgia rheumatica*

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation were provided.

For the diagnosis of polymyalgia rheumatica, Prodigy recommends:

- Hb
- RBC+Hct
- WBC
- Platelets

- CRP
- ESR
- Protein electrophoresis (to rule out multiple myeloma)
- TSH
- CK (to rule out polymyositis and statin-induced myositis)
- For the follow-up, the following tests are recommended:
- CRP
- ESR

#### *4.4.32.3 Giant cell arteritis*

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation were provided.

Lab tests recommended for the diagnosis

- Hb
- RBC+Hct
- WBC
- Platelets
- CRP
- ESR
- For the follow-up, the following tests are recommended:
- CRP
- ESR

#### *4.4.32.4 Spondylitis ankylosans*

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation were provided.

Lab tests recommended for the diagnosis and follow-up:

- Hb
- RBC+Hct
- CRP
- ESR

#### *4.4.32.5 Raynaud phenomenon*

One guideline was available, by Prodigy. No levels of evidence or grades of recommendation were provided.

Lab tests recommended in case of suspicion of connective tissue disorder:

- Hb
- RBC+Hct
- WBC
- Platelets
- CRP

- ESR

### 4.4.33 Osteoporosis, ICPC code L95

One guideline was available, by NHG. No levels of evidence or grades of recommendation were provided.

For patients diagnosed with osteoporosis, the following tests are recommended:

- Alkaline phosphatase
- ESR
- Ca
- TSH
- Phosphate
- Vit D

### 4.4.34 Epilepsy, ICPC code N88

One guideline was available, by Prodigy.

The guideline states that primary care investigations seldom give useful information. To investigate an underlying disorder or metabolic disturbance, tests recommended at the diagnosis of epilepsy:

- Hb
- RBC+Hct
- Glucose
- AST+ALT
- ESR
- Creatinine
- K
- Na
- Ca

Routine monitoring of antiepileptic drugs is not recommended. Indications for monitoring (grade of recommendation D=expert opinion or extrapolation from higher level evidence):

- Non-adherence
- Suspected toxicity
- Adjustment of phenytoin dose
- Management of pharmacokinetic interactions
- Specific clinical conditions, e.g. epileptic status, pregnancy

For the follow-up of adults taking enzyme-inducing drugs, the following tests are recommended every 2-5 years:

- Hb
- RBC+Hct
- AST+ALT
- Alkaline phosphatase
- K

- Na
- Ca
- Vit D

### 4.4.35 Insomnia, ICPC code P06

One guideline was available, by WVVH.

No laboratory tests are recommended in these patients.

### 4.4.36 Alcohol problems, ICPC code P16-16

One guideline was available, by Prodigy.

Although the diagnosis of alcohol problems is made with questionnaires, the following tests may be useful for the diagnosis of liver disease:

- Hb
- RBC+Hct
- Gamma-GT
- AST+ALT
- Alkaline phosphatase
- Total bilirubin

For monitoring progress, the following tests are recommended

- RBC+Hct
- Gamma-GT

### 4.4.37 Dementia, ICPC code P70

Three guidelines were available, by NHG, SIGN and NZGG. No levels of evidence or grades of recommendation were provided.

Tests recommended at the diagnosis of dementia:

| | NHG | SIGN | NZGG |
|---|---|---|---|
| Hb | √ | | √ |
| RBC+Hct | √ | | |
| WBC | | | √ |
| Glucose | √ | | √ |
| ALT | √ | | √ |
| ESR | √ | | √ |
| Creatinine | √ | | √ |
| K* | √ | | √ |
| Na* | √ | | √ |
| Ca* | | | √ |
| TSH | √ | | √ |
| Vit B12 + folate* | √ | | √ |
| Vit B1* | √ | | |
| Vit B6* | √ | | |
| Syphilis serology | | | √ |

* Tests not routinely indicated. K and Na are only recommended during diuretics treatment, and vitamin B1 and B6 in patients with relative malnutrition or alcohol abuse. SIGN states that it is good practice to screen for coexisting medical conditions, but routine testing does not improve diagnostic accuracy. Tests should be selected on clinical grounds according to history and clinical circumstances. NHG always recommends ALT only, and not the combination AST+ALT.

### 4.4.38 Delirium, ICPC code

Two guidelines were available, by NHG and NHG-SAN. No levels of evidence or grades of recommendation were provided.

Tests recommended in patients with acute delirium:

| | NHG | SAN |
|---|---|---|
| Glucose | √ | √ |
| Hb | √* | √ |
| RBC+Hct | √* | |
| WBC | √* | |
| ESR or CRP | √* | √ |
| Creatinine | √* | √ |
| TSH | √* | √ |
| K | √* | √° |
| Na | √* | √° |
| Gamma-GT | √* | √° |
| ALT | √* | √° |
| Ca | √* | √° |

Glucose and urinalysis for nitrate should be done immediately. * Other tests should be selected on clinical grounds.

° Na and K should be tested in case of suspicion of disturbance of the fluid balance. (vomiting, diarrhoea). AST+ALT and gamma-GT should be tested in case of suspicion of liver disease. Ca is tested in patients confined to bed or with bone metastases. Toxicology of digoxin, lithium, theophyllin or tricyclic antidepressants may be useful.

### 4.4.39 Anxiety disorder, ICPC code P74

One guideline was available, by NHG.

No lab tests are recommended in patients with an anxiety disorder.

### 4.4.40 Bipolar disorder, ICPC code P76

Two guidelines were available, by NHG-SAN and NZGG. Levels of evidence or grades of recommendation were not provided.

In patients presenting with a manic episode, the following tests are recommended by NZZG:

- Hb
- RBC+Hct
- Creatinine
- AST+ALT
- Na

- K
- TSH
- Li

Tests recommended in the follow-up of patients taking lithium:

| | SAN | NZZG |
|---|---|---|
| Lithium | √ | √ 12h after last drug dose |
| Creatinine | √ | √ |
| Na | | √ |
| K | | √ |
| TSH | √ | √ |

### 4.4.41 Depression, ICPC code P76

One guideline was available, by Prodigy. Levels of evidence or grades of recommendation were not provided.

Lab tests are not routinely necessary. In patients presenting with predominant fatigue, the following tests may be indicated:

- Hb
- RBC+Hct
- TSH

### 4.4.42 Eating disorders, ICPC code P86

Two guidelines were available, by Prodigy and NZZG.

No lab tests are recommended in patients presenting with eating disorders.

### 4.4.43 Acute cough, ICPC code R05

One guideline was available, by WVVH.

No lab tests are recommended in patients presenting with acute cough.

### 4.4.44 Sore throat, ICPC code R21

Two guidelines were available, by NHG and SIGN.

According to both guidelines, lab tests are routinely not recommended. In case of suspicion of an immunological disorder, NHG recommends:

- WBC
- WBC differentiation

### 4.4.45 Influenza, ICPC code R80

One guideline was available, by Prodigy.

Lab tests are not recommended in patients suspected of or diagnosed with influenza.

### 4.4.46 Acute lower respiratory tract infection, ICPC code R81

Two guidelines were available, by Prodigy and WVVH.

Lab tests are not recommended in patients suspected of or diagnosed with lower respiratory tract infection.

### 4.4.47 Chronic obstructive pulmonary disease, ICPC code R95

Two guidelines were available, by Prodigy and NHG.

According to Prodigy, patients diagnosed with COPD should have the following tests, to check for anaemia or polycythaemia (the latter indicative of chronic hypoxia):

- Hb
- RBC+Hct

No lab tests are recommended in exacerbations of COPD.

### 4.4.48 Asthma, ICPC code R96

Two guidelines were available, by NHG and WVVH.

At the diagnosis of asthma, the following test is recommended:

| | NHG | WVVH |
|---|---|---|
| • RAST | √ | √ (children only) |

### 4.4.49 Allergic rhinitis, ICPC code R98

Two guidelines were available, by Prodigy and NHG.

Only NHG recommends lab testing in patients suspected of allergic rhinitis, in case history is inconclusive:

- RAST

### 4.4.50 Eczema, ICPC code S87

Two guidelines were available, by Prodigy and NHG.

No lab tests are recommended in patients suspected of or diagnosed with eczema.

### 4.4.51 Acne, ICPC code S96

One guideline was available, by NHG.

No lab tests are recommended in patients diagnosed with acne.

### 4.4.52 Venous ulcus, ICPC code S97

One guideline was available, by Prodigy.

The following lab tests are recommended in patients diagnosed with a venous ulcus on the leg:

- Hb
- RBC+Hct
- WBC
- ESR
- CRP
- Glucose
- Creatinine
- Urea
- Na
- K

### 4.4.53 Urticaria, ICPC code S98

One guideline was available, by Prodigy.

In patients with moderate to severe urticaria and in case an environmental trigger such as latex, nuts or fish is considered, the following lab test is recommended

- RAST

If symptoms are problematic, the following tests may be useful:

- Hb
- RBC+Hct
- WBC
- WBC differentiation (eosinophilia may indicate parasite infection)
- ESR (may be raised in vasculitis urticaria)

### 4.4.54 Obesity, ICPC code T82

One guideline was available, by WVVH.

In patients with BMI<30, no lab tests are recommended.

Patients with BMI>30 or increased cardiovascular risk, the following tests are recommended:

- Glucose
- Tot chol
- HDL chol
- Triglycerides

### 4.4.55 Thyroid disorders, ICPC code T85-T86

Three guidelines were available, by Prodigy, NHG-SAN and NHG.

Lab tests recommended in patients suspected of a thyroid disorder:

| | Prodigy | SAN | NHG |
|---|---|---|---|
| TSH | √ | √ | √ |
| Free T4 (if TSH raised) | √ | √ | √ |
| Free T3 (if TSH low) | √ | | |

In patients suspected of subacute thyroiditis, additional tests are recommended:

| | |
|---|---|
| WBC | √ |
| ESR | √ |

Patients suspected of Graves' disease and in pregnant women with a previous hyperthyroidism:

- TSI

Patients treated for hypo or hyper thyroidism, should be monitored with:

| | Prodigy | SAN | NHG |
|---|---|---|---|
| TSH | √ | √ | √ |
| Free T4 | | √ | √ |

### 4.4.56 Diabetes mellitus, ICPC code T89-T90

Five guidelines were available, by Prodigy, SIGN, NHG, WVVH and NZZG.

#### *4.4.56.1 Case finding*

For the detection of patients with diabetes mellitus, the following lab test was recommended:

| | Prodigy | NHG | WVVH | NZZG |
|---|---|---|---|---|
| Glucose | √ | √ | √ (level 2) | √ (grade C) |

•

#### *4.4.56.2 At the time of diagnosis of diabetes mellitus type II*

| | Prodigy | NHG | WVVH | NZZG |
|---|---|---|---|---|
| Glucose | √ | √ | √ | √ |
| HbA1c | | | √ | √ |
| Creatinine | √ | √ | √ | √ |
| K | √ | | | |
| Na | √ | | | |
| Tot chol | √ | √ | √ | √ |
| HDL chol | √ | √ | √ | √ |
| Triglyc | √ | √ | √ | √ |
| LDL | | √ | √ | √ |
| Tot chol/HDL | | √ | | √ |
| TSH | √ | | | |

WHHV assigns level 1 to these recommendations, NZZG grade D.

#### *4.4.56.3 Follow-up of glycaemia control*

All five guidelines recommend the following tests to monitor glyaemic control in both type 1 and type 2 diabetes patients

- Glucose
- HbA1c

#### *4.4.56.4 Annual follow-up*

All five guidelines provide recommendations on the follow-up of patients with diabetes:

| | Prodigy | SIGN | NHG | WVVH | NZZG |
|---|---|---|---|---|---|
| Glucose | √ | √ | √ | √ | √ |
| HbA1c | √ | √ | √ | √ | √ |
| Creatinine | √ | √ | √ | √ | √ |
| K | √ | | √ | | |
| Na | √ | | | | |
| Tot chol | √ | √ | √ | √ | √ |
| HDL | √ | √ | √ | √ | √ |
| Triglyc | √ | √ | √ | √ | √ |
| LDL | | √ | √ | √ | √ |
| Tot chol/HDL | | √ | | √ | |
| TSH | √ | | | | |

In addition to lab tests in blood or plasma, other tests are also recommended, including micro-albuminuria for the screening for diabetic kidney disease.

### 4.4.57 Gout, ICPC code T92

Three guidelines were available, by Prodigy, NHG and NHG-SAN.

For the diagnosis of gout, all three guidelines recommend no lab tests. Uric acid is only recommended at least 4 weeks after the acute phase, in patients suffering from complicated gout (= >attacks over the last year or the presence of tophi).

According to Prodigy, the following tests may be helpful:

- Hb
- RBC+Hct
- WBC
- ESR
- Creatinine to assess renal function
- Gamma-GT, to help assess alcohol intake
- ALT, to help assess alcohol intake

NHG also recommends ESR in case of diagnostic doubt on bacterial arthritis.

All three guidelines recommend the following tests for therapeutic drug monitoring:

- Creatinine, during the uploading phase
- Uric acid, at 3 months

### 4.4.58 Dysuria in older men, ICPC code U01-U02

One guideline was available, by NHG.

Lab tests are not routinely recommended, only urinalysis.

In case of general malaise, suspicion of retention or multiple urinary tract infections, in addition to an ultrasound, the following test is recommended:

- Creatinine

### 4.4.59 Renal failure, ICPC code U28

One guideline was available, by NHG-SAN.

One lab test is recommended in patients suspected of renal failure, or decreased renal function:

- Creatinine

### 4.4.60 Urinary tract infections, ICPC code U71

One guideline was available, by NHG-SAN.

No lab tests are recommended in patients suspected of or diagnosed with a urinary tract infection.

### 4.4.61 Hyperemesis gravidarum, ICPC code W05

One guideline was available, by Prodigy.

The following tests are recommended in severe cases, where there is concern about the health of the mother and the foetus:

- AST+ALT
- Creatinine
- Urea
- Na
- K
- Ca
- TSH

### 4.4.62 Subfertility, ICPC code W15

Two guidelines were available, by Prodigy and NHG-SAN.

The following lab tests are recommended, in addition to other tests such as postcoitum test or semenanalysis:

| | Prodigy | SAN |
|---|---|---|
| Chlamydia ab | √ | √ |
| Progesterone | √ | |
| LH | | √ |
| FSH | | √ |

### 4.4.63 Pregnancy, ICPC code W78

Three guidelines were available, by Prodigy, WVVH and NHG-SAN.

Preconceptual guidance, as recommended by Prodigy:

- HBs Ag
- Rubella IgG

Lab tests recommended at the start of the pregnancy:

| | SAN | WVVH (level of evidence 1-2) |
|---|---|---|
| Serum HCG | √° | |
| Hb | √ | √ |
| RBC+Hct | | √ |
| Glucose | | √# |
| ABO | √ | √ |
| Rh | √ | √ |
| Irregular Ab | √ | √ |
| TSH | √ | √ |
| Free T4 | | √* |
| TSI | | √* |
| Toxo IgM | | √ |
| Toxo IgG | | √ |
| HBs Ag | √ | √ |
| Rubella IgG | √ | √ |
| Hepatitis C Ab | | √ |
| HIV Ab | √ | √ |
| TPPA/TPHA | √ | √ |

° if doubt after urine test

# in case of increased risk or clinical suspicion

* in case of an existing thyroid disorder.

Lab tests recommended at 24 weeks pregnancy, by WVVH (level of evidence 2)

- Hb
- RBC+Hct
- Glucose challenge test
- Irregular Ab

Screening for GBS using vaginal swabs is also recommended.

### 4.4.64 Amenorrhea, I CPC code X05

Two guidelines were available, by Prodigy and NHG.

Lab tests recommended in patients with secondary amenorrhoea:

| | Prodigy | NHG |
|---|---|---|
| TSH | √ | |
| Estradiol | | √ |
| HCG | √ | √ |
| LH | | √ |
| FSH | √ | √ |
| Prolactin | √ | |
| Testosterone | √* | |

* In case of signs of hirsutism or signs of virilization

### 4.4.65 Excessive menstruation, ICPC code X06

Three guidelines were available, by Prodigy, NHG and NZGG.

Lab tests recommended:

| | Prodigy | NHG | NZGG |
|---|---|---|---|
| Hb | √ | √ | √ |
| RBC+Hct | √ | √ | √ |
| WBC | | | √ |
| Platelets | | | √ |

If abnormal, follow algorithm of anemia.

Prodigy grades the recommendation as C-D, NZGG as A.

### 4.4.66 Menopause, ICPC code X11

Two guidelines were available, by Prodigy and NHG.

Lab tests recommended:

| | Prodigy | NHG |
|---|---|---|
| TSH | √ | √ |
| Free T4 | √ | |
| HCG | | √ |
| FSH | √ | |

### 4.4.67 Postmenopausal bleeding, ICPC code X12

One guideline was available, by NHG.

No lab tests are recommended in the diagnosis and management of postmenopausal bleeding.

### 4.4.68 Syphilis, ICPC code X70-Y70

One guideline was available, by NHG-SAN. Levels of evidence or grades of recommendation were not provided.

For the diagnosis of syphilis, the following test is recommended:

- TPHA/TPPA

Patients treated for syphilis, should have the following test 3, 6, 9, 12, 18 and 24 months after treatment:

- VDRL/RPR

### 4.4.69 Gonorrhoea, ICPC code X71-Y71

One guideline was available, by NHG-SAN. Levels of evidence or grades of recommendation were not provided.

For the diagnosis of gonorrhoea, no serum tests are recommended. Diagnosis is made on the basis of microscopy, culture and PCR testing on swabs.

### 4.4.70 Trichomoniasis, ICPC code X73

Two guidelines were available, by NHG-SAN and Prodigy. Levels of evidence or grades of recommendation were not provided.

For the diagnosis of trichomoniasis, no serum tests are recommended. Diagnosis is made on the basis of microscopy and culture on swabs.

### 4.4.71 Bacterial vaginosis, ICPC code X84

One guideline was available, by Prodigy. Levels of evidence or grades of recommendation were not provided.

For the diagnosis of bacterial vaginosis, no serum tests are recommended. Diagnosis is made on the basis of microscopy on swabs.

### 4.4.72 Genital herpes, ICPC code X90-Y72

Two guidelines were available, by Prodigy and NHG-SAN. Levels of evidence or grades of recommendation were not provided.

For the diagnosis of genital herpes, no serum tests are recommended. Diagnosis is made on the basis of culture on swabs.

### 4.4.73 Chlamydia, ICPC code X92

One guideline was available, by NHG-SAN. Levels of evidence or grades of recommendation were not provided.

For the diagnosis of chlamydia, no serum tests are recommended. Diagnosis is made on the basis of PCR testing on swabs or urine.

### 4.4.74 Pelvic inflammatory disease, ICPC code X74

Two guidelines were available, by NHG and Prodigy.

Swabs for detection of Chlamydia and gonorrhoea and a pregnancy test are recommended by both guidelines.

Additionally, NHG recommends the following lab test:

- ESR

### 4.4.75 Prostate cancer, ICPC code Y77

One guideline was available, by NHG-SAN. Levels of evidence or grades of recommendation were not provided.

Lab test recommended in a very selected group of patients, being men with a life expectancy of less than 10 years and a suspicion of prostate carcinoma with metastases:

- PSA

### 4.4.76 Benign prostate hypertrophy, ICPC code Y85

One guideline was available, by Prodigy. Levels of evidence or grades of recommendation were not provided.

In patients suspected of benign prostate hypertrophy, the following lab test is recommended:

- Creatinine (to exclude renal impairment and establish baseline)

## 4.5 DISCUSSION

In this chapter, a large number of clinical practice guidelines was synthesized, representing a large variety of indications for laboratory testing in general practice. But, many of these guidelines are in English, making them relatively impractical for clinicians in Belgium. Domus Medica and SSMG, the two scientific associations of general practitioners in Belgium make considerable efforts to develop guidelines in the two main national languages, but resources are scarce. In addition, recommendations on the use of laboratory for diagnostic purposes, when the target condition of the patient is not yet known, are difficult to find as most guidelines are centred on the target condition. Recommendations based on signs and symptoms to guide the diagnostic process are needed.

Overall, the number of tests that is recommended per indication is limited, ranging from 0 to 16 with an average of little more than 3 tests.

In case more than one guideline was found on the same subject, agreement between recommendations was fair. In addition, the levels of evidence or grades of recommendation were seldom applied, and sometimes contradictory between two guidelines.

Caution needs to be taken to use this synthesis in a normative way. It is by no means possible to conclude that because some tests are not recommended in any of the guidelines, they are not useful in clinical practice. Target conditions that are clinically important because of their high prevalence or high burden on patients, receive more attention from guideline developers, leading to a higher number of guidelines on these target conditions. Other target conditions are underrepresented, by which it is not possible to conclude that some tests are never indicated in general practice, because there were no recommendations found in any of the guidelines.

In addition, patients may present with more than one indication for laboratory testing, leading to higher number of tests per lab request.

### *Key points*

- **Guidelines recommend on average 3 tests per indication, with a range of 0-16.**
- **Levels of evidence or grades of recommendation are seldom applied.**
- **Signs and symptom-based guidelines are needed.**

# 5 PROSPECTIVE STUDY IN GENERAL PRACTICE ON THE MOTIVATION OF LABORATORY TEST UTILISATION

## 5.1 INTRODUCTION

In the first chapter of this report, data were presented on the use of laboratory tests in general practice in Belgium. Although details on patient characteristics were available to a certain extent, the specific indication for a specific test request could not be analysed. But, in order to compare current test requesting behaviour to the recommendations that were found in the guidelines, information on the reason for testing was necessary. Therefore, a prospective study was set up that was designed to explore reasons for testing and would allow comparisons of the current test requesting behaviour with the recommendations from guidelines. In addition, costs could be calculated and simulations of changes in test requesting behaviour on costs were possible.

Thus, the aim of this study was to prospectively analyse a random sample of laboratory test orders of a group of general practitioners in order to assess the choice and volume of ordered tests together with their motivation for ordering these tests (clinical as well as non-clinical motives).

## 5.2 METHODOLOGY

### 5.2.1 Study population

Private laboratories were contacted for participation. Participating GPs were contacted with the laboratories as intermediary. All GPs gave written informed consent to participate in this study. The study was approved by the ethics committee of the scientific association of GPs in Flanders, Domus Medica.

Characteristics of the participating GPs and their practice were collected (age, gender, university of graduation, number of years in practice, urban/country, full-time/part-time, type of practice, involved in vocational training, mean volume of test ordering).

### 5.2.2 Data collection

Each participating GP was asked to answer a separate telephone questionnaire about 20 (randomly selected) test ordering forms that he/she sent to the laboratory during a period of 8 weeks. The anonymous test ordering forms were sent to the researchers by the laboratory immediately after they arrived. The telephone call was made a soon as possible after the tests were ordered (in the majority of cases within 2 days). The questionnaire was drawn up on the basis of evidence from the literature and consensus within the research team. A pilot study with 6 GPs resulted in some minor additions. Tests that were included in the study were the 60 most frequently ordered in general practice (see table 2.1). Tests on urine and requests for pathology (e.g. Papanicalaou stain) were excluded.

For each test ordering form, the following variables were registered: patient age, patient gender, total number of tests ordered, total cost of the tests ordered, cost per test.

Subsequently, the following questions were asked:

- Per test ordering form: why did you decide to perform laboratory tests (short general explanation)
- Per test:

1. You want to exclude a diagnosis. Which one?
2. You want to confirm a diagnosis. Which one?

3. You strongly suspect on clinical basis a certain diagnosis and want to assess the severity through laboratory testing. Which diagnosis?
4. You want to follow-up an existing abnormality:
5. A known abnormality of a laboratory test
6. A known condition. Which one?
7. You want to monitor a treatment? Which one?
8. The patient asked explicitly for this test.
9. Screening in a healthy person
10. Screening on the occasion of laboratory testing for other reasons
11. Screening in patient with vague complaints
12. I want to reassure my worried patient through this test
13. I am worried and need to be reassured
14. I perform this test by order of the medical specialist. Which specialism?
15. I follow a practice guideline? Which one?
16. Other

### 5.2.3 Analysis

All data were entered in SPSS.

Results are described by frequency tables, means and standard deviations where appropriate.

The clinical reasons for testing were ICPC coded where possible. When a condition was mentioned several times but did not have a code in the classification (e.g. chronic renal failure) we attributed a separate code. All clinical reasons were grouped according to the chapters of the ICPC classification, with the exception of conditions mentioned with a high frequency.

## 5.3 RESULTS

### 5.3.1 Characteristics of Laboratories and GPs

In Flanders, two large private laboratories agreed to participate. Both laboratories perform mainly analyses for GPs. In Brussels and the Walloon region of Belgium, three private laboratories agreed to participate. In total 164 GPs participated: 135 in Flanders and 29 in Brussels and the Walloon region. The data were collected from 14-12-2006 until 9-3-2007, resulting in 1579 request forms to be evaluated. The personal and practice characteristics of the participating GPs are summarized in table 5.1.

**Table 5.1: characteristics of participating GPs**

| Personal characteristics | n | % | Range |
|---|---|---|---|
| Gender (male) | 109 | 66.5 | |
| Age (years) | Mean 46.1 | SD 11.6 | 25-79 |
| Involved in education | 57 | 35.4 | |
| Mean number of test orders per month | 62.3 | SD 39.9 | 8 - 219 |
| Years in practice | Mean 20 | SD 11.7 | 0 - 51 |
| University of graduation | | | |
| KUL | 68 | 41.5 | |
| UG | 44 | 26.8 | |
| UCL | 20 | 12.2 | |
| UIA | 16 | 9.8 | |
| ULB | 7 | 4.3 | |
| VUB | 7 | 4.3 | |
| **Practice characteristics** | | | |
| Full time | 148 | 91.4 | |
| solo | 76 | 46.9 | |
| duo | 52 | 32.1 | |
| group | 34 | 21.0 | |
| urban | 54 | 46.9 | |
| rural | 64 | 32.1 | |
| mixed | 44 | 21.0 | |

### 5.3.2 Patient characteristics

Of the 1579 laboratory investigations included in the study, 706 were performed in men and 873 in women (44.7% versus 55.3%). The mean age of the patients was 58.2 years (SD 20.1). Half of the patients were between 45 and 75 years old. On average men were significantly older than women: 59.6 versus 57.2 years (p = 0.016).

### 5.3.3 Laboratory test orders

#### *5.3.3.1 General description*

On average 13.3 tests were requested per test order. The average total cost of one order was 39.4 €, of which 7.3 € paid by the patient. In 18% of the orders only PT/INR were requested. Excluding these orders, the average number of tests became 16.2 with a mean total cost of 44.1 € and 9.1 € for the patient.

The 10 most frequently ordered tests were: Hb, RBC+Hct, WBC, WBC differentiation, AST+ALT, creatinine, glucose, platelets, gamma-GT and total cholesterol. Frequencies for all 60 tests are listed in table 5.2 (see appendix).

#### *5.3.3.2 Reasons for testing*

The main reason for requesting lab tests was in more than half (55.5%) of the cases the follow-up of a chronic condition or treatment. In 20% the main reason was a diagnostic work-up, and about 10% of the requests were performed for general check-up or prevention. Other reasons such as "on request of the patient" (4%) or by "request of a specialist" (0.4%) were less common (see table 5.3).

**Table 5.3: main reasons for laboratory testing**

| | N (%) |
|---|---|
| Follow-up | 876 (55.5) |
| Diagnostic work-up | 310 (19.6) |
| General check-up/prevention | 155 (9.8) |
| Explicit request of the patient | 61 (3.9) |
| Pre-operative examination | 41 (2.6 |
| Worried patient/parent | 29 (1.8) |
| Cardiovascular check-up | 28 (1.8) |
| Pregnancy | 28 (1.8) |
| For insurance/visa/work/school | 19 (1.2) |
| Risk profession/contact (SOA screening) | 10 (0.6) |
| By request of specialist | 6 (0.4) |
| In preparation of consult with specialist | 5 (0.3) |
| Control for sport | 2 (0.1) |

Besides these main reasons, GPs specified additional reasons for requesting tests in almost half (45%) of the orders: one additional reason in 34%, two additional reasons in 9.4%, three in 22 cases (0.1%).

When the main reason was follow-up and an additional reason was mentioned, "by order of a specialist" or "in preparation of a consult with a specialist" was mentioned in 35%, check-up in 28%, and diagnostic work-up in 22%.

In orders with diagnostic work-up as main reason, by far the most frequent additional reason was "follow-up of a chronic condition or treatment" (54%). Others were: check-up (11%), worried patient or parent (11%) and request of the patient (9%).

In orders with "general check-up" as main reason, follow-up is mentioned as additional reason in 54%. Explicit request of the patient (23%) is also important.

**Table 5.4: frequencies of additional reasons**

| Main reason for testing | Diagnostic work-up (%) | Follow-up (%) | Check-up (%) |
|---|---|---|---|
| Total number of additional reasons for testing | 201(100) | 280 (100) | 216 (100) |
| Follow-up | **109 (54)** | | **117 (54)** |
| Diagnostic work-up | | **62 (22)** | 21 (10) |
| General check-up/prevention | 23 (11) | **79 (28)** | |
| Explicit request of the patient | 19 (9) | 11 (4) | **49 (27)** |
| Pre-operative examination | | | 1(0.4) |
| Worried patient/parent | 22 (11) | 4 (1) | 4 (2) |
| Cardiovascular check-up | 7 (4) | 18 (6) | |
| Pregnancy | 6 (3) | 4 (1) | 2 (1) |
| Risk profession/contact (e.g. SOA) | 1 (0.5) | 2 (0.7) | 1(0.4) |
| Request of specialist | 4 (2) | **77 (28)** | 2 (1) |
| In preparation of consult with specialist | 8 (4) | **22 (8)** | 8 (4) |
| Control for sport | | | 1 (0.4) |

### FOLLOW-UP OF A CHRONIC CONDITION OR TREATMENT

In case of follow-up as the main reason for testing, more than one condition is followed in 45% of the patients. In 6% of the cases, even four conditions. The number of

conditions increases significantly with increasing age of the tested patients (Pearson's correlation coefficient 0.39, $p<0.01$).

The most important clinical reasons for follow-up investigations are cardiovascular risk assessment (cholesterol), atrial fibrillation, hypertension and diabetes. However, a great many conditions are mentioned. In total, follow-up is given as reason for testing (main or additional reason) 1915 times (or 1.2 reasons per test order) mentioning 165 different conditions. In the appendix we show all conditions with a frequency of 1% or more (table 5.5).

Apart from follow-up of clinical conditions, therapeutic monitoring is also an important reason for blood testing (25% of reasons for follow-up testing); 75% of these tests is for monitoring anticoagulation therapy.

#### DIAGNOSTIC WORK-UP

In case of diagnostic work-up as the main reason for testing, more than one complaint/working hypothesis was considered in 33% of the patients. In 5%, three complaints/working hypotheses were mentioned.

By far the most frequent diagnostic question was weakness/general fatigue with 20% of test orders. Secondly most common were weight loss and joint symptoms/complaints, each in 4% of orders. In total, diagnostic work-up was given as reason for testing (main or additional reason) 575 times, mentioning 125 different complaints/diagnostic hypotheses. In table 5.6 (appendix) all complaints/diagnostic hypotheses with a frequency of 1% or more are shown.

#### TESTING ON OF A SPECIALIST'S INITIATIVE

In 140 test orders (8%), the GP gives as main or additional reason "by request of a specialist" or "in preparation of a consult with a specialist". In 50% of cases the specialist is an internist, in 17% an oncologist (n=24), in 10% a gynaecologist, in 7% a psychiatrist /neurologist, and in 7% an urologist.

On average a larger number of tests is requested in these orders, but the difference is small and not significant (14.8 versus 13.2; $p = 0.07$).

### 5.3.4 Individual tests

In table 5.7, all tests are listed, detailing the number of requests and the reasons for requesting them (percentages of total for that test).

This table shows that clinical reasons and screening are by far the most important reasons for all tests. Non-clinical reasons such as request of the patient, or for assurance reasons are rather exceptional. Adhering to guidelines is hardly ever a reason for ordering laboratory tests. Remarkably, one of the few tests mentioned in that respect, was fibrinogen. This test was never mentioned in any of the guidelines identified in the previous chapter.

A more detailed analysis of a selection of tests is presented later in this chapter.

**Table 5.7: tests with the general reasons why they were ordered**

| | N | Clinical reason | On patient request | Screening healthy subject | Case finding | Vague complaints | Worried patient | Worried doctor | On specialist request | Guidelines |
|---|---|---|---|---|---|---|---|---|---|---|
| Hb | 1009 | 37.1 | 0.1 | 10.4 | 40 | 3 | 0 | 0.1 | 2 | 0.1 |
| RBC+Hct | 998 | 38.8 | 0.1 | 10.7 | 38.4 | 2.9 | 0 | 0.1 | 2 | 0 |
| WBC | 999 | 29.2 | 0.1 | 10.9 | 41.4 | 11.4 | 0.1 | 0.2 | 2.1 | 0.1 |
| Creatinine | 898 | 36.3 | 0 | 11.1 | 23.8 | 13.9 | 0.1 | 0 | 2.2 | 0.1 |
| Platelets | 833 | 9.6 | 0 | 11 | 57.4 | 15 | 0 | 0.1 | 2.3 | 0.1 |
| WBC different. | 927 | 30.1 | 0.1 | 11.1 | 40.9 | 11.5 | 0.1 | 0.2 | 2.2 | 0 |
| Glucose | 869 | 25.7 | 0.1 | 9.2 | 12.1 | 10 | 0.1 | 0 | 1.6 | 0.1 |
| Gamma-GT | 802 | 48.4 | 0.1 | 12.8 | 23.2 | 12.2 | 0 | 0.2 | 1.9 | 0 |
| AST+ALT | 902 | 48.3 | 0.1 | 11.8 | 22.9 | 12.2 | 0 | 0.2 | 1.8 | 0 |
| CRP | 701 | 42.2 | 0.1 | 8.7 | 33.4 | 10.3 | 0.3 | 0.1 | 1.4 | 0 |
| Urea | 399 | 38.1 | 0 | 12.3 | 22.1 | 14 | 0.3 | 0 | 2.8 | 0.3 |
| K | 461 | 47.9 | 0 | 7.8 | 22.1 | 11.3 | 0.2 | 0 | 2.4 | 0.2 |
| Na | 452 | 47.8 | 0 | 7.3 | 22.6 | 11.3 | 0.2 | 0 | 2.2 | 0.2 |
| Total Chol | 756 | 25.3 | 1.3 | 8.9 | 13.4 | 0.1 | 0 | 0 | 0.9 | 0 |
| Uric acid | 540 | 27.6 | 0 | 9.4 | 11.1 | 11.3 | 0.2 | 0 | 1.1 | 0 |
| Triglycerides | 682 | 28.2 | 1 | 8.8 | 11.3 | 0.4 | 0 | 0 | 0.7 | 0 |
| Alc phosph | 446 | 50 | 0 | 10.3 | 24.2 | 13 | 0 | 0.4 | 2 | 0 |
| HDL chol | 684 | 26.6 | 0.9 | 8.6 | 11.4 | 0.1 | 0 | 0 | 0.6 | 0 |
| TSH | 661 | 45.1 | 0.5 | 11.8 | 37.5 | 1.5 | 0 | 0.2 | 1.1 | 0.2 |
| Cl | 264 | 45.1 | 0 | 7.6 | 25.4 | 11 | 0.4 | 0 | 3 | 0.4 |
| ESR | 726 | 32.8 | 0.1 | 11 | 36.8 | 10.7 | 0 | 0.1 | 1.9 | 0 |
| PT (INR/Quick) | 431 | 88.2 | 0 | 1.4 | 2.3 | 0.2 | 0.2 | 0 | 2.8 | 0.2 |
| Ferritin | 453 | 41.1 | 0.7 | 10.2 | 32.7 | 3.8 | 0.2 | 0 | 1.1 | 0 |
| Ca | 206 | 33 | 0.5 | 10.7 | 34.5 | 18 | 0 | 0.5 | 1.5 | 0 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Fe | 366 | 36.6 | 0.5 | 11.5 | 39.1 | 3.6 | 0 | 0 | 1.6 | 0 |
| Total protein | 276 | 19.6 | 0 | 12.3 | 44.9 | 17.8 | 0 | 0.4 | 1.8 | 0 |
| LDH | 208 | 54.8 | 0.5 | 7.2 | 26.4 | 12 | 0 | 0.5 | 1.9 | 0 |
| Bil tot+fract | 254 | 55.1 | 0 | 7.9 | 24.8 | 9.4 | 0 | 0.8 | 1.6 | 0 |
| FT4 | 236 | 62.7 | 0.4 | 9.3 | 24.2 | 1.3 | 0 | 0.4 | 0.8 | 0 |
| Phosphate | 131 | 38.9 | 0 | 6.1 | 35.1 | 18.3 | 0 | 0.8 | 0 | 0 |
| Amylase | 217 | 23 | 0 | 13.4 | 43.3 | 17.1 | 0.5 | 0.5 | 1.4 | 0 |
| Bicarbonate | 111 | 40.5 | 0 | 7.2 | 27 | 14.4 | 0.9 | 0 | 5.4 | 0 |
| Lipase | 161 | 26.7 | 0 | 14.9 | 36.6 | 19.9 | 0.6 | 0.6 | 1.2 | 0 |
| CK | 129 | 62.8 | 0 | 3.1 | 7.8 | 6.2 | 0.8 | 0.8 | 2.3 | 0 |
| Mg | 109 | 33 | 0.9 | 11.9 | 37.6 | 17.4 | 0 | 0 | 0 | 0 |
| Protein electrophoresis | 137 | 30.7 | 0 | 13.1 | 35.8 | 17.5 | 0 | 0.7 | 0.7 | 0 |
| RAST | 35 | 97.1 | 0 | 0 | 0 | 0 | 0 | 0 | 2.9 | 0 |
| HbA1c | 213 | 80.8 | 0 | 1.4 | 2.8 | 1.9 | 0 | 0 | 1.4 | 0 |
| Vit B12+ folate | 237 | 47.3 | 1.3 | 9.3 | 35 | 3 | 0 | 0 | 0.4 | 0 |
| Fibrinogen | 32 | 46.9 | 0 | 6.3 | 18.8 | 0 | 3.1 | 0 | 9.4 | 3.1 |
| Transferrin | 125 | 45.6 | 0 | 12 | 32.8 | 4 | 0 | 0 | 3.2 | 0 |
| APTT | 31 | 12.9 | 0 | 12.9 | 0 | 0 | 3.2 | 0 | 29 | 3.2 |
| Reticulocytes | 83 | 41 | 0 | 14.5 | 32.5 | 3.6 | 0 | 0 | 2.4 | 0 |
| RF | 44 | 70.5 | 0 | 0 | 13.6 | 9.1 | 0 | 0 | 2.3 | 0 |
| FT3 | 85 | 68.2 | 2.4 | 3.5 | 24.7 | 1.2 | 0 | 1.2 | 1.2 | 0 |
| Bilirubin tot | 21 | 57.1 | 0 | 14.3 | 14.3 | 14.3 | 0 | 0 | 0 | 0 |
| Fe+TIBC/FeSat | 60 | 50 | 0 | 20 | 23.3 | 5 | 0 | 0 | 0 | 0 |
| Toxopl IgG | 27 | 3.7 | 0 | 7.4 | 0 | 0 | 0 | 0 | 3.7 | 0 |
| Toxopl IgM | 25 | 32 | 0 | 4 | 0 | 0 | 0 | 0 | 4 | 0 |
| CMV-IgM | 26 | 46.2 | 3.8 | 3.8 | 0 | 0 | 0 | 0 | 3.8 | 0 |
| HBsAg | 46 | 56.5 | 10.9 | 4.3 | 0 | 0 | 4.3 | 0 | 4.3 | 0 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| HC-Ab | 38 | 65.8 | 15.8 | 2.6 | 0 | 0 | 2.6 | 0 | 5.3 | 0 |
| HIV-Ab | 64 | 54.7 | 35.9 | 6.3 | 0 | 0 | 3.1 | 0 | 3.1 | 0 |
| CMV-IgG | 28 | 10.7 | 3.6 | 7.1 | 0 | 0 | 0 | 0 | 3.6 | 0 |
| Total IgE | 47 | 97.9 | 2.1 | 0 | 0 | 2.1 | 0 | 0 | 2.1 | 0 |
| Estradiol | 13 | 84.6 | 7.7 | 0 | 0 | 0 | 0 | 0 | 7.7 | 0 |
| ABO+Rh | 57 | 0 | 19.3 | 0 | 0 | 0 | 0 | 0 | 3.5 | 0 |
| Progesterone | 12 | 66.7 | 8.3 | 0 | 0 | 0 | 0 | 0 | 8.3 | 0 |
| HBsAb | 36 | 0 | 8.3 | 0 | 0 | 0 | 2.8 | 0 | 2.8 | 0 |
| LH | 14 | 92.9 | 7.1 | 0 | 0 | 0 | 0 | 0 | 7.1 | 0 |

### 5.3.5 Laboratory test orders per clinical indication

In the following section, a more detailed analysis is presented for some of the most common clinical indications that were mentioned by the participating GPs. The requested tests are subsequently compared to the recommended tests for that indication according to the guidelines identified in the previous chapter.

The most common clinical indications for requesting laboratory tests were:

- General check up/ prevention
- Follow-up cardiovascular risk factor (lipid profile)
- Follow-up atrial fibrillation
- Follow-up hypertension
- Follow-up diabetes
- Diagnostic work-up: weakness, general fatigue

Four indications are analysed in detail: general check up/prevention, follow-up of diabetes, follow-up of hypertension and diagnostic work-up for weakness/general fatigue.

#### *5.3.5.1 General check-up/prevention*

In total, "general check-up/prevention" was given as the main reason in 155 laboratory orders. In 25 (16%) this was the only reason; in 130 orders additional reasons were mentioned, totalling 182 additional reasons: 98 (54%) follow-up of a chronic disease or treatment, 45 (25%) explicit request of the patient, 19 (10%) diagnostic work-up and 20 other diverse reasons. (Table 5.8 in appendix)

The follow-up of the lipid profile and hypertension were the most important additional reasons for testing. Other reasons were very diverse and infrequent. None of them could explain the ordering of a specific test with some frequency. Therefore we can conclude that almost all ordered tests were ordered for general check-up, in a number of cases combined with cardiovascular check-up or hypertension.

On average an order for general check-up/prevention contained 21 of the 60 analysed tests (SD 6.1) and cost 50 € (SD 8 €). The personal contribution of the patient was on average 11.5 € (SD 2.6 €).

In table 5.9, all tests with a frequency of >10% are listed. It shows from this table that WBC is the most common test, requested in almost every order for general check-up.

**Table 5.9: frequencies of the different requested tests for reason of general check-up/prevention (tests with frequencies > 10%).**

| | |
|---|---|
| WBC | 98.1 |
| Hb | 97.4 |
| RBC+Hct | 96.1 |
| Total chol | 96.1 |
| Creatinine | 95.5 |
| Glucose | 95.5 |
| AST+ALT | 95.5 |
| WBC differentiation | 93.3 |
| Gamma GT | 92.3 |
| Triglycerides | 91.0 |
| HDL chol | 90.3 |
| Platelets | 87.7 |
| TSH | 78.7 |
| Uric acid | 67.1 |
| ESR | 67.1 |
| CRP | 64.5 |
| Ferritin | 50.3 |
| Alkaline phosphatase | 49.0 |
| K | 47.1 |
| Na | 46.5 |
| Urea | 44.5 |
| Fe | 41.9 |
| Total protein | 39.4 |
| Cl | 34.2 |
| Ca | 29.0 |
| FT4 | 29.0 |
| Vit B12+folic acid | 29.0 |
| Amylase | 27.7 |
| Bilirubin tot+fract | 25.2 |
| LDH | 21.9 |
| Protein electrophoresis | 21.9 |
| Lipase | 19.4 |
| Bicarbonate | 17.4 |
| Phosphate | 16.8 |
| Mg | 16.8 |
| Transferrin | 12.3 |

### COMPARISON TO GUIDELINES

There are no guidelines specifically for routine check-up in patients without complaints. Laboratory testing in healthy persons is generally not recommended. The Dutch guideline "general investigation" is applicable to patients with medical unexplained physical complaints (mups). We assumed that – if a general practitioner decides to perform a general check-up in a person without complaints – the tests recommended by this guideline are a good choice as these tests are chosen to maximise information with a minimal risk of false positive results. (http://nhg.artsennet.nl/uri/?uri=AMGATE_6059_104_TICH_R1634201387349175). In table 5.10 (see appendix) the tests recommended for "general investigation", hypertension and cardiovascular risk calculation are shown.

For mups 6 tests are recommended: Hb, creatinine, glucose, AST+ALT, TSH and ESR. Taking into account possible other reasons for testing (hypertension and cardiovascular risk calculation), at most 14 tests are recommended, including RBC+Hct, total cholesterol, HDL cholesterol, triglycerides, gamma-GT, uric acid, K and Ca.

In 77 of the 155 orders (50%) with as main reason for testing "general check up/prevention"), all 6 recommended tests were requested. In 40 orders tests were lacking: TSH in 47 cases; creatinine, glucose, and AST/ALT in 6 cases, Hb in 3 cases and ESR in 47 cases.

In total, 1501 of the 3248 ordered tests (46%) were not indicated for general check up, follow of hypertension, cardiovascular risk calculation. However, for a number of tests the GP mentioned a specific clinical reason for ordering the test (excluding a diagnosis, confirming a diagnosis, assessing seriousness of a condition, follow-up of a disease, follow-up of therapy). Assuming these tests were indeed appropriate for this reason, the number of inappropriate tests decreased to 1245 or 38%.

**Table 5.11: Tests ordered but not recommended by the guidelines or indicated for other clinical reasons**

| Number of test orders (n=155) | Tests ordered, but not recommended | Tests ordered, not recommended and no other clinical reasons mentioned |
|---|---|---|
| WBC | 152 | 145 |
| Platelets | 136 | 135 |
| WBC Differentiation | 145 | 139 |
| CRP | 100 | 88 |
| Urea | 69 | 58 |
| Na | 72 | 51 |
| Alk phosph | 76 | 67 |
| Cl | 53 | 17 |
| PT (INR/Quick) | 8 | 8 |
| Ferritin | 78 | 67 |
| Fe | 61 | 60 |
| Total protein | 61 | 60 |
| LDH | 34 | 23 |
| Bil tot+fract | 39 | 27 |
| FT4 | 45 | 30 |
| Phosphate | 26 | 21 |
| Amylase | 43 | 42 |
| Bicarbonate | 27 | 17 |
| Lipase | 30 | 29 |
| CK | 13 | 9 |
| Mg | 26 | 19 |
| Protein electroph | 34 | 33 |
| IgE specific | 1 | 0 |
| HbA1c | 38 | 12 |
| Vit B12+folic acid | 45 | 35 |
| Fibrinogen | 5 | 2 |
| Transferrin | 19 | 19 |
| APTT | 0 | 0 |
| Reticulocytes | 18 | 17 |
| Rheuma factor | 4 | 1 |

| | | |
|---|---|---|
| FT3 | 14 | 7 |
| Bilirubine tot | 0 | 0 |
| Fe+ITIBC | 9 | 0 |
| Other | 20 | 7 |
| | 1501 | 1245 |

**FINANCIAL ANALYSIS**

The total cost of all orders (n=155) was 7770 € or 50 € per order (SD 8 €) when considering the 60 analysed tests.

Applying guideline recommendations, the cost of an order limited to the 6 recommended tests would be 24.4 € per order or 3774 € for the 155 orders. Considering 14 tests as appropriate the cost would be 41.6 € per order of 6448 € for 155 orders.

In reality, other tests were added for which other clinical reasons were given. It is not possible to judge whether they were appropriate or not. Assuming they were appropriate, and leaving out on the one hand inappropriate tests (not recommended by guidelines and not ordered for other clinical reasons), and adding on the other hand the cost of the tests lacking according to the guidelines, we found a total cost of 5297 € or 37 € (SD 10 €) per order when 6 tests are considered and 6329 € or 44.3 € (SD 6.9) per order for 14 tests considered appropriate. Costs range from 24 € for an order strictly adhering to the guidelines without additional reasons to 44 € for an order with possible additional reasons. The difference between these two costs is due in part because of the higher number of tests, and in part because of the higher forfaitary reimbursement in the second case.

### *5.3.5.2 Diabetes non insulin dependent*

In 205 laboratory orders the clinical reason for laboratory testing was "non insulin dependent diabetes" or "glucose intolerance".

These orders were made mainly for reason of "follow-up (70 %) of a chronic condition or treatment". Diagnostic work-up was much less frequent (13%) and other reasons were rare (table 5.12, appendix).

In 36 (17%) cases diabetes was the only clinical reason for testing, in 169 orders additional clinical reasons were mentioned. There were 336 additional clinical reasons: 261 (76%) concerned the follow-up of other chronic diseases, 38 (11%) for a diagnostic work-up of other complaints/working hypotheses, and 44 (12%) for therapeutic follow up (mostly anticoagulants in 27 cases and digoxin in 7 cases). (Table 5.13 in appendix)

Cardiovascular diseases are most frequently followed by the same test order as diabetes. Most frequently mentioned were: follow-up lipid profile, non complicated hypertension, atrial fibrillation/flutter, and ischemic heart disease without angina.

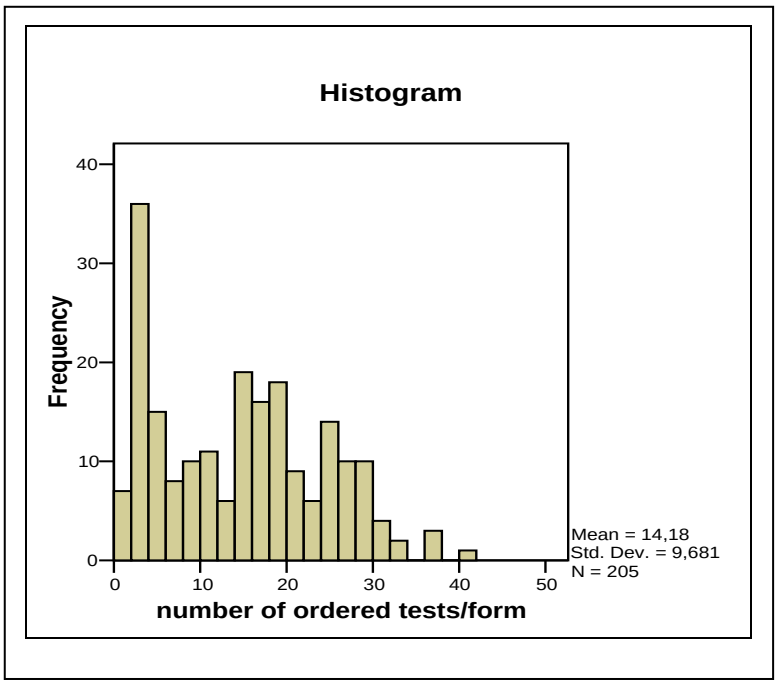
On average an order for diabetes contained 13.5 tests (SD 9.2) and cost 39.5 € (SD 13.6 €). The personal contribution of the patient was on average 7.1 € (SD 5.4 €).

The frequencies of all tests are listed in table 5.14. In 25% of the orders a small number - 4 tests or less - were ordered (see figure 5.1). These orders usually consisted of glucose, HbA1c and/or PT/INR.

**Table 5.14: frequencies of the different tests in orders with as clinical reason for testing "non insulin dependent diabetes" or "glucose intolerance" (>10%).**

| | % |
|---|---|
| Glucose | 92.2 |
| HbA1c | 82.0 |
| Creatinine | 66.8 |
| Hb | 62.4 |
| RBC+HCT | 62.0 |
| WBC | 62.0 |
| AST+ALT | 56.6 |
| Differentiation WBC | 55.1 |
| Total chol | 54.6 |
| Platelets | 52.7 |
| Triglycerides | 51.2 |
| HDL chol | 49.3 |
| Gamma GT | 47.3 |
| ESR | 44.9 |
| CRP | 42.4 |
| Uric acid | 41.5 |
| K | 40.5 |
| Na | 40.0 |
| TSH | 37.1 |
| Urea | 28.8 |
| Alkaline phosph | 26.8 |
| Ferritine | 25.4 |
| Cl | 22.4 |
| Fe | 20.0 |
| Ca | 16.6 |
| PT (INR/Quick) | 16.1 |
| Total protein | 16.1 |
| Bil tot+fract | 13.7 |
| Vit B12+folic acid | 13.7 |
| LDH | 12.7 |
| FT4 | 12.2 |
| CK | 11.7 |

**Figure 5.1: frequency of the number of ordered tests per order form for diabetes**




## COMPARISON TO GUIDELINES

In table 5.15 (appendix), tests recommended for diabetes and for the common additional indications (hypertension, follow-up lipid profile/cardiovascular risk calculation an atrial fibrillation/flutter) are shown.

For the follow-up of diabetes 9 tests are recommended: glucose, HbA1c, creatinine, total cholesterol, HDL cholesterol, triglycerides, K, Na, and TSH. Taking into account the additional frequent reasons for testing, 18 tests would be appropriate: Hb, RBC+Hct, gamma-GT, AST+ALT, CK, uric acid, Ca, PT/INR, APTT.

Only in 28 of the 205 orders (13.7%) with as clinical reason "diabetes, non insulin dependent or glucose intolerance", all 9 recommended tests were requested. Since the 9 tests are only indicated for annual follow-up or diagnosis, we excluded the smaller orders (≤ 4 tests), which were possibly intended for monitoring glycaemic control. In the 152 larger orders, all 9 recommended tests were present in 18.4 % of the test orders. In total, 414 tests were lacking according to the guidelines (table 5.16).

Na, K and TSH are only recommended in one guideline whereas glucose, creatinine, total cholesterol, triglycerides, HDL cholesterol and HbA1c are recommended in the majority of the guidelines. These 6 tests were all present in 49 % of the larger orders. When considering these 6 tests, according to the guidelines, 196 tests are lacking.

Two tests are recommended in the guidelines for all diabetes indications (diagnosis, follow-up, monitoring glycaemic control). These 2 tests were both present in 74% of the test orders: glucose was tested in 92.2% and HbA1c in 82%. Thirty-two tests (12 glucose and 20 HbA1c) should have been ordered and were lacking.

**Table 5.16: frequency of the 9 recommended tests in tests orders for diabetes (with number of tests ≥ 4) N=152**

| | N | % |
|---|---|---|
| Glucose | 144 | 94.7 |
| Creatinine | 132 | 86.8 |
| HbA1c | 129 | 84.9 |
| Tot chol | 111 | 73 |
| Triglyc | 104 | 68.4 |
| HDL | 100 | 65.8 |
| K | 82 | 53.9 |
| Na | 81 | 53.3 |
| TSH | 75 | 49.3 |

In total 1728 of the 2781 ordered tests (62.1 %) were not recommended for diabetes according to the guidelines. Taking into account the additional cardiovascular reasons the number of non recommended tests became 1108 or 39.8 %. For a number of tests the GP mentioned a specific (other) clinical reason for ordering the test (excluding a diagnosis, confirming a diagnosis, assessing seriousness of a condition, follow-up of a disease, follow-up of therapy). Assuming these tests were appropriate for this reason, the number of inappropriate tests became respectively 1083 or 38.9% (for 9 appropriate tests) and 736 or 26.5 % (for 18 appropriate tests).

**Table 5.17: frequency of tests not recommended by the guidelines or not ordered for other clinical reasons.**

| Total number of ordered tests (n=2781) | Tests not recommended for diabetes | Tests not recommended for diabetes and no other indications mentioned | Tests not recommended for DM and CV diseases | Tests not recommended for DM and CV diseases and no other indications mentioned |
|---|---|---|---|---|
| Hb | 128 | 98 | | |
| RBC+HCT | 127 | 93 | | |
| WBC | 127 | 103 | 127 | 103 |
| Platelets | 108 | 98 | 108 | 98 |
| WBC differentiation | 113 | 90 | 113 | 90 |
| Gamma GT | 97 | 39 | | |
| AST+ALT | 116 | 48 | | |
| CRP | 87 | 60 | 87 | 60 |
| urea | 59 | 39 | 59 | 39 |
| Uric acid | 85 | 68 | | |
| Alk phosph | 55 | 22 | 55 | 22 |
| Cl | 46 | 17 | 46 | 17 |
| ESR | 92 | 64 | 92 | 64 |
| PT (INR/Quick) | 33 | 2 | | |
| Ferritin | 52 | 45 | 52 | 45 |
| Ca | 34 | 19 | | |
| Fe | 41 | 34 | 41 | 34 |
| Total protein | 33 | 27 | 33 | 27 |
| LDH | 26 | 10 | 26 | 10 |
| Bil tot+fract | 28 | 11 | 28 | 11 |
| FT4 | 25 | 12 | 25 | 12 |
| Phosphate | 20 | 8 | 20 | 8 |
| Amylase | 19 | 13 | 19 | 13 |
| Bicarbonate | 19 | 7 | 19 | 7 |
| Lipase | 14 | 7 | 14 | 7 |
| CK | 24 | 5 | | |
| Mg | 18 | 10 | 18 | 10 |
| Protein electrophoresis | 18 | 13 | 18 | 13 |
| IgE specific | 1 | 0 | 1 | 0 |
| Vit B12+folic acid | 28 | 17 | 28 | 17 |
| Fibrinogen | 2 | 0 | 2 | 0 |
| Transferrin | 14 | 11 | 14 | 11 |
| APTT | 1 | 0 | | |
| Reticulocytes | 6 | 6 | 6 | 6 |
| Rheuma factor | 7 | 2 | 7 | 2 |
| FT3 | 7 | 5 | 7 | 5 |
| Bilirubin tot | 6 | 1 | 6 | 1 |
| Fe+ITIBC | 4 | 1 | 4 | 1 |
| Other | 8 | 3 | 8 | 3 |
| | 1728 | 1108 | 1083 | 736 |

**FINANCIAL ANALYSIS**

Considering all orders, the total cost of the test orders for reason of diabetes for the 60 analysed tests was 8092 € or 39.5 €/ order.

The 152 larger orders (> 4 tests) represented in total 6897 € or 45.4/ order.

The cost of an order limited to the 9 recommended tests would cost 40.4 €/ order or 6132 € for the 152 larger orders. Leaving out on the one hand all inappropriate tests (not recommended by guidelines and not ordered for other clinical reasons), and adding on the other hand the costs of the tests lacking according to the guidelines, we found the following results summarized in table 5.18.

**Table 5.18: financial scenarios**

| | | **total cost of orders for diabetes (> 4 test /order) N=152** |
|---|---|---|
| 9 tests are appropriate** | 6 tests are necessary* | 6151 € or 40.7 €(SD 6.0)/ order |
| | 9 tests are necessary* | 6318 € or 41.8 € (SD 5.6) / order |
| 18 tests are appropriate*** | 6 tests are necessary* | 6445 € or 42.6 € (SD 5.9) / order |
| | 9 tests are necessary* | 6583 € or 43.4 € (SD 5.6) / order |

*In cases where these tests were lacking the cost of the tests was added

** according to the guidelines, 9 tests can be considered appropriate, and 6 tests are recommended in the majority of the guidelines

***"Appropriate" when taking into account the other frequent clinical indications for testing

### *5.3.5.3 Hypertension*

In 184 laboratory orders the clinical reason for laboratory testing was "hypertension".

These orders were made mainly (51%) for the "follow-up of a chronic condition or treatment". "General check up" and "diagnostic work-up" were mentioned in respectively 20% and 14%. Other reasons were rare (table 5.19 in appendix).

In 21 cases (11%) hypertension was the only clinical reason for testing, in 163 orders additional clinical reasons were mentioned. There were 322 additional clinical reasons: 245 (76%) concerned follow-up of other chronic diseases, 54 (17%) diagnostic work-up of other complaints/working hypotheses, in 23 (7%) follow up of medication.

**Table 5.20: additional reasons for testing besides hypertension (classified according to ICPC classification)**

| **Additional clinical reasons for follow-up (N=245)** | | **N (%)** |
|---|---|---|
| Cardiovascular | Lipid metabolism | 80 (32.7) |
| | Other | 22 (9.0) |
| Endocrine/metabolic and nutritional | Diabetes/glucose intolerance | 36 (14.7) |
| | Other | 35 (14.3) |
| Musculoskeletal | | 19 (7.8) |
| Digestive | | 12 (4.9) |
| Psychological | | 12 (4.9) |
| Blood/blood forming organs and immune mechanism | | 9 (3.7) |
| Respiratory | | 4 (1.6) |
| Urological | | 4 1.6) |
| Female genital | | 4 (1.6) |
| Male genital | | 4 (1.6) |
| Skin | | 2 (0.82) |
| General/unspecified | | 1 (041) |
| Neurological | | 1 (0.41) |
| **Additional clinical reasons for diagnostic work-up (N=54)** | | |
| Cardiovascular | | 9 (16.7) |
| Musculoskeletal | | 9 (16.7) |
| General/unspecified | | 9 (16.7) |
| Endocrine/metabolic and nutritional | | 7 (13.0) |
| Digestive | | 6 (11.1) |
| Neurological | | 4 (7.4) |
| Respiratory | | 3 (5.6) |
| Psychological | | 2 (3.7) |
| Blood/blood forming organs and immune mechanism | | 1 (1.9) |
| Urological | | 1 (1.9) |
| Female genital | | 1 (1.9) |
| Male genital | | 1 (1.9) |
| Skin | | 1 (1.9) |
| **Follow-up of medical treatment (N=23)** | | |
| Anticoagulants | | 10 (43.5) |
| Start ACE inhibitor | | 4 (17.4) |
| Digoxin | | 3 (13.0) |
| Other | | 6 (26.1) |

Cardiovascular diseases, namely lipid metabolism, and diabetes are the most frequently diseases followed by the same test order as diabetes. The other clinical reasons are very diverse and have all very low frequencies.

On average, orders for hypertension contained 17.2 tests (SD 8.1) of the 60 analysed tests and this cost 47.6 € (SD 12.7 €). The personal contribution of the patient was on average 9 € (SD 5 €).

**Table 5.21: frequencies of the different tests in orders with as clinical reason for testing "hypertension" (>10%).**

| N = 182 | N (%) |
|---|---|
| Creatinine | 179 (97.3) |
| Hb | 166 (90.2) |
| Wbc | 164 (89.1) |
| Glucose | 164 (89.1) |
| AST+ALT | 164 (89.1) |
| RBC+Hct | 163 (88.6) |
| Total chol | 151 (82.1) |
| Differentiation WBC | 147 (79.9) |
| Gamma-GT | 147 (79.9) |
| Triglycerides | 142 (77.2) |
| HDL chol | 138 (75.0) |
| Platelets | 136 (73.9) |
| K | 135 (73.4) |
| Na | 133 (72.3) |
| CRP | 122 (66.3) |
| TSH | 120 (65.2) |
| Uric acid | 115 (62.5) |
| ESR | 113 (61.4) |
| Alk phosph | 93 (50.5) |
| Urea | 79 (42.9) |
| Ferritine | 79 (42.9) |
| Fe | 73 (39.7) |
| Cl | 68 (37.0) |
| Total protein | 59 (32.1) |
| Bil tot+fract | 55 (29.9) |
| Ft4 | 45 (24.5) |
| Amylase | 44 (23.9) |
| Vit b12+folic acid | 44 (23.9) |
| Hba1c | 43 (23.4) |
| LDH | 42 (22.8) |
| Ca | 40 (21.7) |
| Protein electroph | 29 (15.8) |
| Lipase | 28 (15.2) |
| Carbonate | 24 (13.0) |
| CK | 23 (12.5) |
| Mg | 22 (12.0) |
| PT (INR/quick) | 21 (11.4) |

In table 5.15 (appendix), tests recommended for hypertension, and for the frequent additional indications, follow-up lipid metabolism/cardiovascular risk calculation and diabetes are shown.

For the follow-up of hypertension 12 tests are recommended: Hb, RBC+Hct, glucose, creatinine, total chol, HDL chol, triglycerides, gamma-GT, uric acid, K, Na, TSH and Ca. Eight tests are recommended by more than one guideline. Taking into account the

other frequent clinical indications CK, AST+ALT and HbA1C may be considered appropriate as well.

In 30 of the 184 orders (16.3%) with as clinical reason "hypertension", all 12 recommended tests are ordered. In total 530 tests are lacking according to the guidelines.

TSH, Triglycerides, gamma-GT and calcium are recommended in only one guideline while creatinine, glucose, haemoglobin, RBC+Hct, tot cholesterol, HDL cholesterol, Ka and Na are recommended in more guidelines. These 8 tests were all present in 88 (48%) of the orders. When considering these 8 tests, according to the guidelines 243 tests are lacking.

**Table 5.22: frequencies of recommended test (N=184)**

| | N | % |
|---|---|---|
| Creatinine | 179 | 97.3 |
| Hb | 166 | 90.2 |
| Glucose | 164 | 89.1 |
| RBC+Hct | 163 | 88.6 |
| Tot chol | 151 | 82.1 |
| Gamma-GT | 147 | 79.9 |
| Triglyc | 142 | 77.2 |
| HDL chol | 138 | 82.1 |
| K | 135 | 73.4 |
| Na | 133 | 72.3 |
| TSH | 120 | 65.2 |
| Ca | 40 | 21.7 |

In total 2373 of the 3597 ordered tests (66%) were not recommended for hypertension according to the guidelines. Taking into account the additional reasons for testing CK, AST+ALT and HBA1c may be considered appropriate. In this case the number of inappropriate tests became 2144 or 59.6 %.

For a number of tests the GP mentioned a specific (other) clinical reason for ordering the test (excluding a diagnosis, confirming a diagnosis, assessing seriousness of a condition, follow-up of a disease, follow-up of therapy). Assuming these tests were appropriate for this reason, the number of inappropriate tests became 1513 (42.1%) or 1404 (39%) (When accepting CK, AST+ALT and HBA1c as appropriate).

**Table 5.23: frequency of tests not recommended by the guidelines or not ordered for other clinical reasons.**

| Total number of ordered tests (n= 3597) | Number of tests not recommended for hypertension | Number of tests not recommended for hypertension and no other indications mentioned |
|---|---|---|
| WBC | 164 | 139 |
| Platelets | 136 | 127 |
| Differentiation WBC | 147 | 125 |
| Gamma GT* | 147 | 73 |
| AST+ALT | 164 | 82 |
| CRP | 122 | 88 |
| Urea | 79 | 24 |
| Uric acid | 115 | 84 |
| Trglycerides* | 147 | 89 |
| Alk phosph | 93 | 41 |
| TSH* | 120 | 77 |
| Cl | 68 | 13 |
| ESR | 113 | 85 |
| PT (INR/quick) | 21 | 8 |
| Ferritine | 79 | 60 |
| Ca* | 40 | 23 |
| Fe | 73 | 58 |
| Total protein | 59 | 53 |
| LDH | 42 | 20 |
| Bil tot+fract | 55 | 27 |
| Ft4 | 45 | 21 |
| Phosphate | 18 | 10 |
| Amylase | 44 | 36 |
| Carbonate | 24 | 4 |
| Lipase | 28 | 22 |
| CK | 22 | 15 |
| Mg | 18 | 10 |
| Protein electrophoresis | 29 | 22 |
| Ige specific | 1 | 0 |
| Hba1c | 43 | 12 |
| Vit B12+folic acid | 44 | 33 |
| Fibrinogen | 8 | 4 |
| Transferrine | 13 | 12 |
| APTT | 2 | 2 |
| Reticulocytes | 9 | 8 |
| RF | 3 | 0 |
| Ft3 | 17 | 8 |
| Bilirubine tot | 6 | 1 |
| Fe+ITIBC | 5 | 4 |
| Other | 10 | 2 |
| | 2373 | 1513 |

*recommended by one guideline

**FINANCIAL ANALYSIS**

Considering all orders, the total cost of the test orders hypertension for the 60 analysed tests was 8759 € or 47.6 €/ order.

The cost of an order limited to the 12 recommended tests would cost 40.3 €/ order or 7333 for the 184 orders. An order limited to the 8 tests recommended in more than one guideline would cost 24.2 € or 4453 €.

Allowing for the uncertainty on the appropriateness of additional tests for which clinical reasons were given, the various financial scenarios are listed in table 5.25, leaving out on the one hand inappropriate tests (not recommended by guidelines and not ordered for other clinical reasons), and adding on the other hand the costs of the tests lacking according to the guidelines.

**Table 5.24: financial scenarios**

| | | **total cost of orders for hypertension N=174** |
|---|---|---|
| 8 test recommended** | 8 tests necessary* | 6784 € or 36.8 € (SD 8.9)/ order |
| 12 tests recommended** | 8 tests necessary* | 7480 € or 40.7 € (SD 7.3)/ order |
| | 12 tests necessary* | 7619 € or 41.4 € (SD 6.8) /order |
| 15 tests appropriate*** | 8 tests necessary* | 7678 € or 41.7 € (SD 7.2) / order |
| | 12 tests necessary* | 7810 € or 42.4 € (SD 6.8) / order |

*In cases where these tests were lacking the cost of the tests was added

** according to the guidelines,

***"Appropriate" when taking into account the other frequent clinical indications for testing

### *5.3.5.4 Weakness/general fatigue*

In 121 laboratory orders "weakness/general fatigue" was given as one of the mean reasons for performing the test.

In none of these orders this was the only reason. There were in total 220 additional reasons: 119 (54%) diagnostic work-up, 45 (25%) follow-up of a chronic disease or treatment, 24 (10%) explicit request of the patient, 38 (16 %) other diverse reasons.

All the clinical reasons for testing besides weakness/fatigue were very diverse and infrequent. None of them could explain the ordering of a specific test with some frequency.

In table 5.26 the frequencies of the different tests ordered for "weakness/fatigue" are shown.

**Table 5.25: frequencies of the different requested tests for reason of weakness/fatigue (tests with frequencies > 10%).**

| | N | % |
|---|---|---|
| Hb | 120 | 99.17 |
| RBC+HCT | 117 | 96.69 |
| WBC | 117 | 96.69 |
| WBC differentiation | 110 | 90.91 |
| AST+ALT | 105 | 86.78 |
| Creatinine | 104 | 85.95 |
| TSH | 102 | 84.30 |
| Platelets | 98 | 80.99 |
| Glucose | 95 | 78.51 |
| Gamma-GT | 94 | 77.69 |
| CRP | 87 | 71.90 |
| ESR | 84 | 69.42 |
| Totaal chol | 77 | 63.64 |
| Ferritine | 77 | 63.64 |
| HDL chol | 68 | 56.20 |
| Triglycerides | 61 | 50.41 |
| Uric acid | 55 | 45.45 |
| Alkaline phosphatase | 55 | 45.45 |
| Urea | 54 | 44.63 |
| Fe | 54 | 44.63 |
| K | 47 | 38.84 |
| Na | 47 | 38.84 |
| Vit B12+folic acid | 44 | 36.36 |
| Total protein | 33 | 27.27 |
| FT4 | 32 | 26.45 |
| Amylase | 28 | 23.14 |
| Cl | 26 | 21.49 |
| Lipase | 25 | 20.66 |
| Transferrine | 25 | 20.66 |
| Ca | 24 | 19.83 |
| LDH | 24 | 19.83 |
| Bil tot+fract | 21 | 17.36 |
| Phosphate | 19 | 15.70 |
| Protein electrophoresis | 18 | 14.88 |
| Mg | 16 | 13.22 |
| Fe+ITIBC | 16 | 13.22 |

On average an order for weakness/fatigue contained 19 of the 60 analysed tests (SD 6.9) and cost 49 € (SD 9.5 €). The personal contribution of the patient was on average 11 € (SD 23.4 €).

There are no evidence-based guidelines specifically on laboratory testing for "weakness/tiredness, general". Literature shows that blood testing seldom offers an explanation for this complaint (http://www.ssmg.be/new/files/RBP_Fatigue.pdf). The Dutch guideline "general investigation" is intended for patients with medical unexplained physical symptoms i.e. vague complaints without obvious physical cause such as

weakness/tiredness. Therefore we assume that this guideline is applicable to patients with weakness/tiredness. (See table 5.10 in appendix):

Six tests are recommended: Hb, creatinine, glucose, AST+ALT, TSH and ESR. In 51 of the 121 orders (48.7%) with as main reason for testing weakness/fatigue, all 6 recommended tests were requested. In 62 orders tests were lacking: TSH was lacking in 43 cases; creatinin in 17 cases, glucose in 26 cases, AST/ALT in 46 cases, Hb in 1 case and ESR in 21 cases.

In total 1723 of the 2333 ordered tests (74%) were not recommended for weakness/fatigue.

However, for a number of tests the GP mentioned a specific clinical reason for ordering the test (excluding a diagnosis, confirming a diagnosis, assessing seriousness of a condition, follow-up of a disease, follow-up of therapy). Assuming these tests were indeed indicated for this reason, the number of non-indicated and non-recommended tests decreased to 1027 or 44 %.

**Table 5.26: Tests ordered but not recommended by the guidelines or indicated for other clinical reasons**

| Number of test orders N=155 | Number of tests ordered, but not recommended | Number of tests ordered, but not recommended and no other clinical reasons mentioned |
|---|---|---|
| RBC+HCT | 117 | 1 |
| WBC | 117 | 83 |
| Platelets | 98 | 97 |
| WBC differentiation | 110 | 77 |
| Gamma-GT | 94 | 64 |
| CRP | 87 | 55 |
| Urea | 54 | 47 |
| K | 47 | 37 |
| Na | 47 | 36 |
| Total chol | 77 | 71 |
| Uric acid | 55 | 49 |
| Triglycerides | 61 | 54 |
| Alk phosph | 55 | 37 |
| HDL chol | 68 | 63 |
| Cl | 26 | 23 |
| PT (INR/quick) | 5 | 1 |
| Lipase | 77 | 22 |
| Ferritine | 24 | 3 |
| Ca | 54 | 21 |
| Fe | 33 | 3 |
| Total protein | 24 | 28 |
| LDH | 21 | 14 |
| Bil tot+fract | 32 | 12 |
| FT4 | 19 | 0 |
| Phosphate | 28 | 16 |
| Amylase | 10 | 26 |
| Carbonate | 25 | 10 |
| CK | 12 | 6 |
| Mg | 16 | 11 |
| Protein electroph | 18 | 15 |
| Ige specific | 5 | 0 |
| Hba1c | 7 | 4 |
| Vit B12+folic acid | 44 | 0 |
| Transferrine | 25 | 1 |
| Fe+ITIBC | 16 | 0 |
| Other | 115 | 40 |
| TOTAL | 1723 | 1027 |

**FINANCIAL ANALYSIS**

The total cost of all orders (n=121) was 5985 € or 49.4 € per order (SD 9.5) when considering the 60 analysed tests.

The cost of an order limited to the 6 recommended tests would cost 24.4 € / order or 2946 € for the 121 orders.

Allowing uncertainty on the appropriateness of tests for which clinical reasons were given, and leaving out on the one hand inappropriate tests (not recommended by guidelines and not ordered for other clinical reasons), and adding on the other hand the cost of the tests lacking according to the guidelines, we found following results summarized in table 5.28.

**Table 5.27: financial scenario**

| | | **total cost of orders for check-up N=155** |
|---|---|---|
| 6 test** recommended | 6 tests necessary* | 4994 € or 41,28 € / order (SD 8.47) |

*In cases where these tests were lacking the cost of the tests was added

## 5.3.6 Analysis of individual tests

Comparing the frequencies of the individual tests to the guidelines (table 5.7), a number of tests was ordered quite frequently in spite of the fact that they are hardly ever indicated. Examples are urea, total protein, amylase, platelets and chloride.

In this paragraph the reasons for ordering these tests will be analysed in more detail.

### *5.3.6.1 Urea*

Urea was ordered in 399 or 25.3% of all orders.

The motivations for these orders are summarized in table 5.28 (appendix). Urea is requested for follow-up in 40% of the cases, and for a diagnostic work-up in 26%. In comparison to the main motivations in the whole sample, follow-up of a chronic disease or treatment was somewhat less frequent and check-up was more frequent.

In all, 660 clinical reasons (for follow-up or diagnostic work-up) for performing the laboratory tests were given. (Table 5.29 in appendix) The most frequent reason was "follow-up of lipid profile", but a great many very diverse other reasons are also mentioned. The clinical reasons for laboratory orders containing urea are very similar to clinical reasons mentioned in the whole sample.

Looking at the motivations for specifically ordering urea, it was found that "screening" was the reason for ordering this test in more than half of the cases, followed by clinical reasons in almost 40%. Taking a closer look at the clinical reasons for specifically ordering urea, renal pathology (25%), diabetes (18%) and follow-up of a treatment with diuretics (23%) were the most common reasons.

In the guidelines testing for urea is indicated in:

- Hiccups
- Hyperhidrosis
- Heart failure
- Treatment with ACE inhibitors
- Diagnosis of rheumatoid arthritis
- Venous leg ulcer
- Hyperemesis gravidarum

In 52 cases or 13 % of the orders with urea, ordering of urea can be considered appropriate: 32 tests were requested for the follow-up of a treatment with ACE inhibitors, 9 for heart failure, 6 for rheumatoid arthritis, 4 for gout and 1 for hyperhidrosis.

In conclusion, urea is most frequently ordered for screening – an indication for which it is not recommended. Also, in most of the clinical conditions mentioned by the GPs as reason for ordering this test, it was not indicated according to the guidelines. Only a minority of tests for urea could be considered appropriate.

#### *5.3.6.2 Total protein*

Total protein was ordered in 276 or 17.5% of all orders.

The main reasons for these 276 orders were follow-up in 33% and diagnostic work-up in 29%. Check-up or prevention was mentioned in 22% of the orders. In comparison with the main motivations in the whole sample, follow-up of a chronic disease or treatment is less frequent and diagnostic work-up and check-up is more frequent.

In these orders, 493 clinical reasons for performing the laboratory tests were given (table 5.30 in appendix). The most frequent reasons were the diagnostic work-up of "weakness/general fatigue", "follow-up of hypertension", "lipid metabolism" and "diabetes". The clinical reasons for laboratory orders with total protein are very similar to the clinical reasons in the whole sample.

Looking at the motivations for specifically ordering total protein, "screening" was the reason for ordering this test in almost 70% of the cases, followed by clinical reasons in 24%. All other reasons were mentioned in less than 5% of the cases.

In only 19 % a clinical reason specific for total protein was given. The most frequent were "inflammation" (34%) and "vitamin, nutritional deficiency" (25%).

In conclusion, total protein is most frequently ordered for screening. General practitioners mention very few specific clinical reasons for ordering this test. In none of the mentioned reasons total protein is indicated in general practice. Therefore all orders of total protein can be considered as inappropriate.

#### *5.3.6.3 Amylase*

Amylase was ordered in 217 or 13.7% of all orders.

The motivation for these orders was for follow-up in 31%, for a diagnostic work-up in 29% and for check-up in 26%. In comparison with the main reasons in the whole sample, follow-up of a chronic disease or treatment is less frequent, diagnostic work-up and check-up are more frequent.

In these orders, 423 clinical reasons for requesting laboratory tests were given. The most frequent reason was "follow-up of lipid metabolism", but a great many very diverse other reasons were also mentioned. The clinical reasons were again similar to the most common clinical reasons in the whole sample. (see table 5.31 in appendix). Digestive problems and endocrine/metabolic/nutritional problems represented respectively 11% and 16% of all clinical reasons for these blood tests.

Looking at the motivations for specifically ordering amylase, screening was the reason for ordering this test in almost 70% of the cases, followed by clinical reasons in 26%. As could be expected, pancreas pathology was the most common reason (n=49). Therapeutic follow-up and chronic alcohol abuse were second most common (n=5 each) and mononucleosis and diabetes were each mentioned once.

None of the existing guidelines recommends the measurement of amylase. At this moment no guidelines were available on pancreatitis for general practice. Pancreatitis is an uncommon disease in general practice. Screening for pancreas pathology by measuring amylase in patients without specific complaints is not useful.

In our sample at most 49 or 22.5 % of all amylase tests may be considered appropriate. However, this would imply that pancreatitis is present or suspected in 3% of all tested patients of the entire sample.

### *5.3.6.4 Platelet count*

Platelet count was ordered in 833 or 52.8 % of all orders.

The motivations for these orders were follow-up in 38%, diagnostic work-up in 28% and check-up in 16%. As for the other tests in the previous paragraphs, in comparison with the main reasons for all orders, follow-up of a chronic disease or treatment was less frequent, diagnostic work-up and check-up were more frequent.

In these 833 orders, 1569 clinical reasons for performing the laboratory tests were given. The most frequent reason was "follow-up of lipid metabolism", "hypertension" and "diabetes", but a great many very diverse other reasons were also mentioned. The clinical reasons were again similar to the most common clinical reasons for the whole sample. Diseases of the blood or blood forming organs were in 8 % of the orders a clinical reason for testing. (See table 5.32 in appendix)

Looking at the motivations for specifically ordering a platelet count, screening was the reason for ordering this test in more than 80 % of the cases. Clinical reasons were mentioned in 7%.

Only in 80 orders or 9.6 % a specific clinical reason for ordering a platelet count was given. In all cases this was for therapeutic monitoring (n=80), sometimes in combination with a disease (n=21). The kind of medication for which platelet counts were requested varied. In 42 of the 80 cases a platelets count could be considered appropriate given the type of medication (myelo- or haematotoxic).

In the guidelines counting of platelets is recommended in following conditions:

- Hyperhidrosis
- Treatment with myelotoxic drugs
- Heparin therapy
- Anemia
- Increased bleeding tendency
- TIA
- Reumatoid arthritis
- Excessive menstruation

Except for the use of myelotoxic drugs, none of these conditions was given as clinical reason for counting platelets in the investigated laboratory orders.

In conclusion, ordering a platelet count is mainly done for screening. In a minority of cases the test is ordered for follow-up of potentially toxic medication and/or haematological diseases. Only 5% of the orders for platelet counts can be considered as appropriate.

### *5.3.6.5 Chloride*

Chloride was ordered in 264 or 16.7 % of all orders.

The motivation for these orders was follow-up in 41%, diagnostic work-up in 23% and check-up in 20%. In comparison with the main reasons for all orders, again follow-up of a chronic disease or treatment was less frequent, diagnostic work-up and check-up were more frequent.

In these 264 orders, 577 clinical reasons for performing the laboratory tests were given. The most frequent reason was again "follow-up of lipid metabolism", "hypertension"

and "diabetes" but a great many very diverse other reasons were also mentioned. The clinical reasons were comparable to those of the entire sample. (Table 5.33 in appendix)

Looking at the motivations for specifically ordering chloride, clinical reasons (43%) and screening (42%) were the main reasons.

In 119 orders or 45.1 % a specific clinical reason for ordering chloride was given. In the majority of cases this was therapeutic monitoring (n=80), mainly diuretics (n=55) and ACE inhibitors (n=39) (more than one therapeutic drug was possible). 58 diseases were mentioned, the most important being "electrolyte disturbances" (n=26) and "renal pathology" (n=14).

In conclusion, chloride was mainly ordered for screening and follow-up of a medical treatment, especially diuretics. In none of these cases it was recommended.

## 5.4 DISCUSSION

As was shown in this prospective study, most laboratory tests were requested for clinical reasons and on the general practitioner's initiative. Non-clinical reasons for testing or testing on the patient's or specialist's request were rather rare.

The motivations for requesting laboratory tests were complex. Often tests were performed for more than one reason. Vague complaints, co-morbidity and prevention all played a prominent part in test ordering. This reflects very well the complexity of general practice itself.

The choice of tests was mostly not in agreement with recommendations from guidelines: many ordered tests were not indicated, some tests were unjustly left out. Even when taking into account all other possible clinical reason for performing the test, there is still room for quality improvement in the choice of tests.

A number of tests were ordered quite frequently while they were hardly ever indicated in general practice. The reason for ordering these tests was in the majority of cases "screening". Leaving out these tests will decrease the cost of laboratory testing and more importantly, improve quality. Requesting laboratory tests in healthy subjects is possibly harmful, as abnormal test results will occur just by chance. These abnormal test results can lead to inappropriate additional testing or treatment, and induce anxiety in patients.

The potential for lowering health expenditure by improving test ordering behaviour is lower than one could expect when considering the guidelines, because of the complexity of clinical reasoning in one patient for which laboratory tests are performed. In many cases several guidelines are applicable, and additional reasons for laboratory testing may exist not yet covered in guidelines.

One of the strengths of the study was the assessment of reasons for testing in 'real life' and not on case vignettes. In addition, a large number of GPs agreed to participate in the study, leading to a high number of test orders that could be included in the study. Recall bias was minimized by the short interval between test ordering and interview. But, on the other hand, participation was voluntarily and it can be assumed that especially GPs with an interest in the use of laboratory tests and quality assurance volunteered to participate. Also, there was always the chance of retrieving 'socially acceptable' answers and the risk of the study itself influencing the GPs test ordering behaviour. The effect of these risks would be that the results would be influenced in a positive direction, in other words, test requests would seem more appropriate than in reality.

*Key points*

- **General practitioners request laboratory tests most for the follow-up of a chronic illness, for diagnostic reasons or for check-up**
- **More than one reason for requesting laboratory tests was present in most cases**
- **Better adherence to guidelines would improve quality: some tests would decrease, others would increase**
- **Screening of healthy subjects with laboratory tests is common, using multiple non-indicated tests**
- **Although costs per test order could lower to only a fair extent, the total costs of all laboratory testing could lower substantially.**

# 6 INTERVENTIONS TO INFLUENCE LABORATORY TESTS ORDERING

## 6.1 INTRODUCTION

Multiple interventions have been designed to influence laboratory testing behaviour of physicians over the last decades. With these interventions, researchers tried to decrease the number of tests requested or to adjust inappropriate test requesting behaviour into more appropriate behaviour.

Audit and feedback are the most common strategies to improve clinical practice. Jamtvedt[25] defined audit and feedback as "any summary of clinical performance of health care over a specified period of time, given in a written, electronic or verbal format". The effectiveness of audit and feedback appears intuitive, because healthcare professionals would be prompted to modify their practice behaviour if given feedback that their clinical practice was inconsistent with that of their peers or accepted guidelines[26]. But, the effectiveness of audit and feedback has been questioned. Organisational strategies also appear to be useful, for example, the utilisation of a restricted prescription form or the implementation of financial interventions.

This chapter aims to respond to the following research question: Which interventions are most efficacious to change the current situation to a more optimal one, on laboratory test requesting behaviour by general practitioners? Therefore, we summarized the available evidence on interventions that can modify the prescription of laboratory tests in general practice.

## 6.2 METHODOLOGY

The literature review followed the basic search procedure of the Belgian Health Care Knowledge Centre. The literature was searched in two steps; the first step was a search for good quality systematic review and the second step was an update of any identified review.

The search terms used for the first step were: "diagnostic test$.and behavior modif$" combined with (Primary Health Care/) AND (Diagnostic Tests, Routine/ or "Laboratory Techniques and Procedures"/). The search was subsequently limited to systematic reviews in Medline from 1990 to September 2006. A similar search string was used in Embase.

For organisational interventions, studies were identified in a third step, in Medline from 1996 to September 2006, using the terms 'laboratory utilization.mp.' AND 'routine.mp.'.

In addition, the reference lists of the selected articles were searched for any missing relevant publications.

Studies were included in case they reported studies on interventions aimed at modifying general practitioners' laboratory tests utilization. Studies were excluded in case they related to theoretical aspects, were performed in a hospital setting, and evaluated prescribing practices other than laboratory tests. Studies selected at this stage were assessed on quality using the checklists developed by the Cochrane Collaboration, and available from www.cochrane.nl. See appendix for more details.

One study[14] was excluded because of lack of quality. The participants were not randomised but selected using unclear selection criteria; furthermore it described the effect of an educational intervention from only one person.

Data were extracted from the original studies, focusing on the effectiveness of the various interventions.

## 6.3 RESULTS

The first step retrieved one systematic review [27] of sufficient quality. (See appendix for quality appraisal). In the second and third steps, studies focused on primary care and published between 01/01/1998 (which is the end of the literature search for the systematic review by Solomon et al.) and September 2006 were selected. From those original studies, 17 were initially selected based on title and abstract for further review on full text. After evaluation for eligibility according to the inclusion and exclusion criteria, 12 articles were finally selected for review (see table 6.1 in appendix).

Five trials describe several types of interventions aimed to implement guidelines in general practice: (Baker, Flottorp, Verstappen, Thomas,and Winkens) and one based on computer-based decision support (van Wijk). In addition, six organisational interventions were evaluated. In the Netherlands[20 21 28] and the United Kingdom[19], four interventions were based on a modification of the content or the design of the prescription forms. For financial interventions, two were focused on laboratory tests solely (van Walraven and Kerr).

### 6.3.1 Systematic review

The aim of the review published by Solomon in JAMA was to evaluate interventions improving laboratory test utilization by all physicians (all specialties). The review was performed for the years 1966 to January 1, 1998, and identified 102 articles (English-language). After quality appraisal, 49 original studies remained. The methodological quality of this review itself is high but methodological flaws in the original articles included in the review hamper drawing strong conclusions (level of evidence 1 a).

The authors categorise interventions in predisposing, enabling and reinforcing interventions. Predisposing interventions are targeted at the physician's knowledge, for example educational interventions. Enabling interventions are resources or structural barriers, for example problem-oriented request forms or reimbursement changes. Finally, reinforcing interventions reward a specific behaviour, for example by receiving feedback.

In this review, reduced volume or charges of laboratory testing was reported in 76% of studies. Interventions targeted at many behavioural factors were more successful (86%) than studies aimed at a single behavioural factor (62%). Absolute effect measures were not available from this review.

The interventions targeted at many behavioural factors used a variable combination of strategies, but included almost all: conference and/or audit and feedback (about volume and charge), and/or guideline dissemination, and/or reminder, and/or requiring justification, and/or test order form revised. Based on this review, we may conclude that a majority of interventions to improve physicians' testing practices claimed success, while nearly every strategy has had both success and failure in all settings, providing limited guidance for designing new or more effective strategies.

### 6.3.2 Update of the systematic review

#### *6.3.2.1 Guideline implementation and feedback*

No studies were identified that evaluated the effect of guideline implementation alone. All studies used combined strategies, for example using the guidelines as a basis of feedback provision.

Of all the studies published between January 1998 and September 2006, two studies failed to show a significant benefit from the intervention: the study of Baker[29] and the study of Flottorp.

The Baker study, where the lead general practitioner of each practice was asked to distribute feedback copies to the others GPs, failed to show change in the number of tests requested despite of 4 episodes of feedback in a 12-month period (level of evidence 1b).

The cluster randomised trial of Flottorp[30] combined passive diffusion of guidelines (without feedback) followed by computer based decision support and reminders, which led to a small decrease (5%) in the use of urinalysis (p= 0,046). In the process evaluation of this study, Flottorp suggests that inadequate time, resources and support were the most important factors explaining a lack of success from the intervention. Based on these results, we may conclude that more personalised or more intensive strategies may be required (level of evidence 1b)

Other studies consisting of a multifaceted strategy combining guidelines, reminders, conferences and audit with feedback, did achieve positive results. Verstappen et al. report the results of an RCT in which primary care physicians discussed personal feedback related to 3 EBM-guidelines in small groups during 6 months. Arm A received intervention about 3 clinical problems, being cardiovascular topics and upper and lower abdominal complaints and arm B about 3 other, being chronic obstructive pulmonary disease and asthma, general complaints and degenerative joint complaints. Each arm acted as a control for the other. In group A the total number of tests for clinical problems allocated to arm A decreased by 12% while there was no change in the control group (decrease of 67 tests more per physician in arm A than in arm B, 95% CI -104 to -30) (P= 0.01). In the intervention group B the total number of tests for clinical problems allocated to arm B decreased by 8% whereas tests decreased by 3% in the control group (decrease of 28 tests per physician, 95%CI -74 to +14) (P = 0.22) (level of evidence 1b).

Thomas et al. designed a cluster randomised controlled trial to evaluate enhanced feedback and brief educational reminder messages on nine tests over a 1 year period. Practices received feedback, reminder messages or both. They were significantly less likely to request the target tests than the control group: the odds ratio for feedback was 0.87 (95%CI 0.81 - 0.94), the odds ratio for reminders was 0.89 (95%CI 0.83 - 0.93), the odds ratio for the combination of feedback and reminders was 0.78 (95%CI 0.71 - 0.85). The effect varied across the targeted tests individually. The two strategies (feedback and reminders) were effective alone and in combination, but neither intervention was consistently better than the other (level of evidence1b).

A long time intervention during 9 years was performed in Maastricht (the Netherlands)[16], consisting of continuous 6-monthly personalised feedback based on guidelines, which showed a 45% decrease for 44 common tests from 1984 to 1993 (mean annual decrease 6%, p<0.001) in the intervention group. The control group showed a 3.2% annual increase in test ordering (level of evidence 2a). Based on this study, we may conclude that when feedback is repeated and continuous (general learning effect), effects are sustained and even progressive.

#### *6.3.2.2 Computer-based support*

One RCT has compared the efficacy of two computer-based interventions used in the Netherlands. One group used a restricted prescription form (BloodLink-Restricted) and the other group a version based on guidelines (BloodLink-Guidelines)[17]. GPs who used BloodLink-Guidelines requested 20% fewer tests on average than did practitioners who used BloodLink-Restricted (mean [±SD], 5.5 ± 0.9 tests vs. 6.9 ± 1.6 tests; p<0.003). Decision support based on guidelines is more effective in changing blood-test ordering than is decision support based on initially displaying a limited number of tests (level of evidence 1b). It should be noted that the authors stress the importance of the context, as the introduction of BloodLink was facilitated by the fact that GPs were already using computer-based patient records.

#### *6.3.2.3 Prescription form modification*

The Netherlands have tested several models of prescription forms. In a small (47 GP in the intervention group, 28 in the control group) randomised controlled trial, the number of tests decreased with 18% after the introduction of a restricted list, but this decrease was not sustained after the old form was reintroduced[20] The periods differ significantly, but this is totally due to the intervention period (p<0.001) (level of evidence 2a).

Smithuis[28] also achieved a significant reduction in the prescription of 3 tests (on a total of 6) by using a restricted form(level of evidence 1b). Nevertheless, this study took place in a region which had already received an intervention with a problem oriented prescription form two years earlier.

Van Gend[21] performed a study on a restricted prescription form accompanied by 6-monthly feedback. This before-after study achieved a reduction of 23% of tests ordered( level of evidence 2b).

In the UK, similar results (no total available) were found by Bailey et al.[19] (level of evidence 2b).

In conclusion, the utilisation of a restricted prescription form alone or in combination with other interventions may be effective to achieve a substantial reduction in the number of tests requested.

#### *6.3.2.4 Financial interventions*

From the articles that were identified in the literature search, only two were solely focused on laboratory tests. In a retrospective study performed in Canada, of fairly low quality[31], 3 interventions were combined: guidelines, laboratory requisition form modification and changes to funding policy (stop funding of total thyroxine). The study showed a decrease of 58% for urea tests and a switch from iron test to ferritin (80% decrease of iron tests). Thyroxine and TSH also decreased but the difference found was not statistically significant (level of evidence 3).

Another study performed in New Zealand[32] combined the same interventions: guidelines, use of restricted prescription forms and financial incentives. The GPs of one practice were allowed to use the financial gain of reducing test ordering for other aspects of their clinical practice. This intervention showed an overall savings of 22.7% in laboratory costs over a period of 13 months (level of evidence 2a). The primary intervention group had a decrease of 32.9%, but the control group also showed an overall decrease in the mean of laboratory costs by 20.3%. But, variability between physicians increased in the control group.

Based on these two studies, we conclude that comprehensive strategies including financial interventions may be effective in certain forms of care delivery systems.

#### *6.3.2.5 Comparisons*

Only one study[33], already cited above, made a comparison between two strategies but failed to show an advantage for one strategy over another: the two strategies evaluated (feedbacks and reminders) were effective alone and in combination.

## 6.4 DISCUSSION

From this review, it shows that a majority of interventions to improve physicians' testing practices can claim limited success.

Audit, individual feedbacks and peer review provide knowledge to physicians on what to do and insight into one's own performance. Most recent studies showed efficacy for interventions that were intensive and well adjusted to the local context. Long time interventions appear to show positive and even progressive results. This emphasizes the necessity of maintaining interventions once they have started.

The results of computer decision support are promising. It is a potentially effective method requiring relatively little effort, provided computer-based medical records are widely used [34].

The introduction of a restricted list appears to be effective to decrease the number of tests, but this decrease is reversible after the old form is re-introduced.

In recent studies, financial interventions were always combined with other strategies. All studies on such organizational interventions were performed in a graded health care

with access to secondary care on referral by the general practitioner. Therefore, the acceptability of such strategies may be questioned in the Belgian context.

It is difficult to choose between various strategies because only one study makes a comparison between two strategies. Studying cost consequences of various interventions may be helpful. Poley et al. installed a computer-based guideline-driven decision-support system (CDSS) in 118 primary practices in the Netherlands and calculated the costs of the intervention in this group. The total intervention costs amounted to 79,000 euro or 670 euro per practice. The introduction of CDSS reduced the number of blood tests per order form and achieved a saving on the costs of laboratory requests of 847 euro per practice every 6 months. Verstappen [10] studied cost effects of the intervention described on 4.3.2. This study compares cost for arm A (topics: cardiovascular topics and upper and lower abdominals complaints) receiving multifaceted strategy with cost for arm B receiving only traditional feedback strategy. Multifaceted strategy combined feedback, education on guidelines, and quality improvement sessions in small quality groups. The intervention costs 93 Euro per physician per 6 months in the complete intervention arm (A). The mean costs reduction that physicians in that arm achieved by reducing unnecessary tests was 144 Euro larger per physician per 6 months than the physicians in the feedback arm B ($p=0.048$). Based on these studies, we may conclude that providing electronic decision support for ordering blood tests in primary care represents an economically promising concept. But, the studies did not discuss the risk of harms for the patients and were focused on a reduction of the number of tests requested, and not on appropriate test ordering behaviour which could imply an increase in some tests as well.

Several studies theoretically discussed the risk of harms: theirs authors argue that the interventions were based on guidelines which are guarantors for quality of care. Indeed those risks make intrinsically part of the guideline development process and must have been balanced there. Only one study studied a possible effect of test request reduction on hospital admission rates. In the study by Winkens et al. in which 64 GPs [35] received routine feedback on test ordering behaviour, a reduction in diagnostic test use was not accompanied by a higher hospital referral rate, not even for specialties related to tests discussed in the feedback. In contrast, poor responders to the feedback showed increased referral rates, as opposed to good responders whose hospital referral rates decreased ($p<0.01$).

This review shows similarities to a previous study performed by the Federal Knowledge Centre in 2005 in order to evaluate the impact of feedback on the prescription rate of antibiotics [36]. From the results of that literature review, it became apparent that changes in physician behaviour are difficult to obtain and that there is no strategy that has been proven to be efficacious in all situations. Adapting the interventions to the local situation is necessary. Multifaceted interventions are considered more efficacious by some [37], but this has not been proven as yet [25]. Solomon, in conclusion of her review and despite a lack of significant difference, suggests that such strategies appear to be more effective. Even when an intervention is efficacious, the absolute effects are generally limited [25]. The notion of interventions targeted at many behavioural factors as described by Solomon et al. [27] is similar to these multifaceted interventions [37]. Several important and rigourous reviews were not included in this review, as it was restricted to general practice. However, the results of these reviews are very similar to what has been found here. Grimshaw et al. reported in their last review that current guideline dissemination and implementation strategies can lead to improvements in care within the context of rigorous evaluative studies. However, they argue that there is an imperfect evidence base to support decisions about which guideline dissemination and implementation strategies are likely to be efficient under different circumstances.

## 6.5 CONCLUSIONS

It shows from the literature that interventions such as audit and feedback, computer-based decision support and financial incentives may be useful in changing physician's behaviour in laboratory test utilisation. But they should be:

- well designed and organised
- based on guidelines
- part of a continuous process
- adapted to the local context

***Key points***

- **The majority of interventions (feedbacks, computer-reminders and/or financial incentives) to improve physicians' testing practices have limited effectiveness.**
- **Feedback must be repeated and continuous (general learning effect) in order to achieve a progressive and sustained result.**
- **The results of computer decision support are promising in settings where computer-based medical records are widely used.**
- **Comprehensive strategies including financial interventions may be effective in certain forms of care delivery systems.**
- **It is difficult to choose between various strategies by lack of conclusive studies**

# 7 GENERAL DISCUSSION

In this report, various aspects of laboratory testing in general practice have been studied.

It shows from the data that laboratory tests are used increasingly in general practice over the last decades. The increase is partly due to an increase in patients needing tests as could be expected considering the aging population. Some tests declined, for example rheuma factor test or total T4.

Generally, guidelines are to be considered the criterion by which appropriateness of testing is measured. But, as was shown in our chapter on guideline synthesis, many guidelines do not apply levels of evidence or grades of recommendations on laboratory tests recommendations, even when they do so for therapeutic recommendations. Partly, this may be explained by the paucity of good quality evidence that is setting-specific. This paucity leads inevitably to variation in recommendations and even contradictory results. For the clinician, recommendations on the same topic that are not fully in agreement are confusing. In addition, clinicians need recommendations that are adapted to their local context, and recommendations from countries with large differences in health care organisation or different prevalence of diseases may not be applicable to their clinical practice.

One important conclusion that can be drawn from the prospective study is that general practitioners mostly have multiple reasons for ordering laboratory tets in a patient. The follow-up of chronic conditions or therapies was the main reason, but many orders had both a diagnostic, follow-up, and screening objective. Ordering laboratory tests at the patient's request was less common, although more prominent in a general check-up. Comparing actual test ordering behaviour to the guidelines, it was shown that many tests are requested unnecessarily and others are not requested although they are recommended. In general, better adherence to guidelines would result in considerable immediate cost saving. But, effects on the patient could be even more important. Theoretically, the more tests are requested, the higher the chance for a false positive result. Abnormal test results are either rechecked some time later, induce immediate treatment or are simply ignored. Thus, false positive results are always costly: even ignored they create unnecessary costs to the health insurance but more importantly, they may create burden to the patient in terms of unnecessary treatment or repeat testing. In conclusion, if tests requests would comply with guidelines better than they do now, substantial costs and burden for patients could be prevented.

Although changing habits is not easy, it was shown from our review that interventions have been shown to be successful in reducing tests. Multiple strategies may be more efficacious. It is fair to assume that these interventions are cost-effective: they cost less than what they save.

GPs are not fully aware or do not take into account the financial consequences of testing. They request those tests they consider necessary, not influenced by reimbursement or expenses for the patient or society. In the appendix of this report, a simulation of costs for the health insurance and the laboratory is presented. Although data for this simulation were collected in a university-based hospital laboratory, some conclusions may be applicable to private, ambulatory laboratories. The costs and income for laboratory tests are difficult to estimate, due to the reimbursement structure in Belgium. A decrease in tests requests will probably result in an increase in costs per test, which is to be expected considering the cost-volume relation. Secondly, the impact of stepwise testing on the costs and profit of the laboratory was simulated. In stepwise testing, one or a few tests are ordered first, and additional tests are ordered on the same blood sample according to the results of the first tests. Stepwise testing may introduce changes in income and costs: requesting an additional test costs the laboratory approximately 3 Euros, although costs could be substantially lower in case of automatic laboratory-based algorithms. But, in some cases, input from the treating physician will be necessary. For example in the anaemia algorithm, different tests are requested in patients with or without a chronic condition. In the two case studies, being

anaemia and thyroid testing, the effect on profit for the laboratory was similar: one algorithm led to a marginal increase in profit while reducing costs for the health insurance; in the other algorithm, profit was reduced by 2% while equally reducing the costs for the health insurance. These examples show that effects on profit are lower than the reduction in cost for the social security. Caution should be taken in interpreting these results for several reasons: First, a number of assumptions were made in order to allow the simulations. Whether or not these assumptions hold could not be tested within the constraints of this project. Secondly, data were used of a laboratory with a fairly large proportion of hospitalised patients, providing highly specialised care. It is to be expected that results might be different in private, ambulatory laboratories. Although analyses using data from such laboratories would have been preferable, they were not possible due to the unavailability of such data. Thirdly, only two case studies were considered to simulate the costs and income for stepwise testing. Other algorithms may provide different results. Finally, as was shown in the prospective study in primary care, general practitioners often have multiple reasons for requesting laboratory tests, by which the number of tests requested increase and simulations become more complicated.

For the purpose of this report, group discussions with GPs were held on the topic of laboratory testing. GPs point out that training and education on laboratory testing is often oriented towards specialist care, although setting specific information is vital in diagnostics. As shown in numerous publications, the value of a diagnostic test can differ tremendously between settings. After graduation, the main source of information for the GP is the laboratory itself. Although valuable, some limitations and problems may arise when the laboratory is used as sole source of information. Firstly, it is unclear where the information is based upon, and whether it is up to date and adapted to the GP's setting. Secondly, laboratories have an implicit conflict of interest, as their profit is dependent on the numbers of test orders and individual tests requested by it. Thirdly, GPs specifically stated to need information on clinical pathways, starting from the signs and symptoms of the patient, information not readily available in the laboratories.

Indeed, patients do not enter the practice with diagnostic label already attached to their forehead. Evidence on clinical pathways is emerging, also from general practice itself. It is to be expected that these pathways will gain importance over the following years. But, it is not to be expected that clinicians can keep track of these developments. GPs are not familiar with the interpretation of diagnostic test estimates, especially not if multivariable or meta-analyses have been done. In this respect, guideline developers have an important task of giving more weight to the diagnostic pathways, incorporating the latest evidence in practice based recommendations.

# 8 POLICY RECOMMENDATIONS

- General practitioners require independent, scientifically reliable and easily accessible information on the appropriate use of laboratory tests.
- A national guideline on the use of laboratory tests in general practice, also starting from signs and symptoms and including pre-analytical aspects, is needed urgently. The scientific organisations of general practice in Belgium should treat developing such a guideline as a priority. Collaboration with clinical biologists would be advisable.
- Integration of this information with the clinical practice is mandatory. This may be achieved by personalised feedback.
- A problem-oriented order form with a restricted list of tests would decrease inappropriate tests and increase appropriate tests. Using computer decision support, this form may be integrated with the electronic medical record and the national guideline.
- Awareness of the costs of laboratory testing should be increased, both costs for the health care insurance as for the patient. Again, computer based decision support systems may be programmed to show these costs.
- Students in medical training should be taught how to use laboratory tests judiciously, also during vocational training.

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# 10 APPENDIX

# CHAPTER 2 THE USE OF LABORATORY TESTS IN BELGIUM

**Table 1. RIZIV/INAMI use of selected laboratory tests per nomenclature number between 1995 and 1999**

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|---|---|---|
| allergy | RAST | 438115 | Bepalen van specifieke IgE per antigeen (Maximum 6) (Cumulregel 47) Klasse 13 | 837160 | 1029556 | 932892 | 813135 | 658544 |
| | | 556275 | Bepalen van specifieke IgE per antigeen (Maximum 6)(Cumulregel 47) Klasse 13 | | | 103284 | 324175 | 516628 |
| | total IgE | 438093 | Doseren van IgE totaal (Maximum 1) (Cumulregel 46) Klasse 13 | 234808 | 300703 | 263723 | 218770 | 163701 |
| | | 556253 | Doseren van IgE totaal (Maximum 1)(Cumulregel 46) Klasse 13 | | | 58239 | 141462 | 199407 |
| anemia | ferritin | 433090 | Doseren van ferritine (Maximum 1) (Cumulregel 305) Klass | 750535 | 956043 | 924683 | 808939 | 496357 |
| | | 541472 | Doseren van ferritine met niet isotopenmethode (Maximum 1) (Cumulregel 305) Klasse 13 | 372813 | 619780 | 745137 | 1082225 | 1561211 |
| | Folic acid | 433053 | Doseren van foliumzuur in het serum (Maximum 1) (Cumulregel 303) Klasse 13 | 21363 | 25980 | 27214 | 28224 | 23297 |
| | | 541435 | Doseren van foliumzuur in het serum met niet isotopenmethode (Maximum 1) (Cumulregel 303) Klasse 13 | 7353 | 13018 | 8952 | 17043 | 29336 |
| | Folic acid eryhtrocytes | 433075 | Doseren van foliumzuur in de erythrocyten (Maximum 1) (C | 55042 | 68331 | 66851 | 69801 | 60463 |
| | | 541450 | Doseren van foliumzuur in de erythrocyten met niet isotopenmethode (Maximum 1) (Cumulregel 304) Klasse 14 | 8300 | 18042 | 21147 | 32170 | 50245 |
| | Iron | 540551 | Doseren van ijzer (Maximum 1) (Cumulregel 15) Klasse 9 | 1299413 | 1716033 | 1842855 | 2020315 | 2120992 |
| | Iron & RBC | 540573 | Doseren van ijzer en bepalen van het ijzerbindend vermogen (Maximum 1) (Cumulregel 15, 16) Klasse 11 | 736829 | 895792 | 732371 | 714981 | 672866 |
| | transferrin | 541030 | Doseren van transferrine met een immunologische methode (Maximum 1) (Cumulregel 16) Klasse 9 | 339822 | 463628 | 515418 | 557901 | 600034 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|---|---|---|
| | Vit B12 | 433112 | Doseren van vitamine B12 (Maximum 1) (Cumulregel 303) Klasse 13 | 57194 | 73993 | 75066 | 81530 | 65767 |
| | | 541494 | Doseren van vitamine B12 met niet isotopenmethode (Maximum 1) (Cumulregel 303) Klasse 13 | 16134 | 31399 | 34247 | 46740 | 77841 |
| | Vit B12 & folic acid | 433134 | Doseren van vitamine B12 en foliumzuur (Maximum 1) (Cumulregel 303) Klasse 16 | 263014 | 333346 | 327696 | 337788 | 262307 |
| | | 541391 | Doseren van vitamine B12 en foliumzuur, met niet isotopenmethode (Maximum 1) (Cumulregel 303) Klasse 16 | 49605 | 90879 | 108299 | 161991 | 282834 |
| cardiovascular | HDL-cholesterol | 540293 | Doseren van HDL-cholesterol (Maximum 1) (Cumulregel 13) Klasse 10 | 2058061 | 2734637 | 2846704 | 3190435 | 3319078 |
| | LDL-cholesterol | 542231 | Doseren van LDL-cholesterol, met uitsluiting van berekeningsmethoden (Maximum 1)(Cumulregel 13) (Diagnoseregel 54) Klasse 14 | | | | | 14787 |
| | Total cholesterolerol | 540271 | Doseren van totale cholesterol (Maximum 1) Klasse 6 | 2522463 | 3265571 | 3335391 | 3650762 | 3767367 |
| | triglycerides | 541376 | Doseren van triglyceriden (Maximum 1) Klasse 8 | 2285862 | 3002078 | 3079121 | 3410238 | 3541223 |
| coagulation | INR/Quick | 554573 | Thromboplastinetijd (prothrombinetijd) (Maximum 1) (Cumulregel 54) Klasse 6 | 1288950 | 1713588 | 1763603 | 1917480 | 2069385 |
| | PTT | 554676 | Geactiveerde gedeeltelijke thromboplastinetijd (Maximum 1)(Cumulregel 107) Klasse 8 | | | 352304 | 533352 | 602245 |
| diabetes | C-peptide | 434173 | Doseren van C-peptide (Maximum 1) (Cumulregel 322, 89) Klasse 16 | 32100 | 41971 | 43523 | 49031 | 50538 |
| | | 559134 | Doseren van C-peptide (Maximum 1)(Cumulregel 89, 322) Klasse 16 | | | | | |
| | glucose | 120050 | Doseren van glucose (Maximum 1) (Cumulregel 1) Klasse 3 | 7790 | 9602 | 8129 | 5238 | 5022 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|---|---|---|
| | | 125053 | Doseren van glucose (Maximum 1) (Cumulregel 3) Klasse 3 | 2933712 | 3809819 | 3877780 | 4203626 | 4366458 |
| | Glucose (+4) | 120190 | Glucosedagcurve (minimum 4 doseringen), inclusief de eventuele doseringen van de glucosurie (Maximum 1)(Cumulregel 1) Klasse 18 | | | 1 | 378 | 400 |
| | | 125193 | Glucosedagcurve (minimum 4 doseringen), inclusief de eventuele doseringen van de glucosurie (Maximum 1)(Cumulregel 3) Klasse 18 | | | 23658 | 29563 | 25350 |
| | Hb gly | 540750 | Doseren van glycohemoglobine in hemolysaat (Maximum 1) (Cumulregel 18) (Diagnoseregel 56) Klasse 13 | 483506 | 633567 | 665504 | 728401 | 777294 |
| | Hyperglycemia curve | 120153 | Curve van verwekte hyper- of hypoglycemie (minimum vier doseringen), inclusief de eventuele doseringen van de glucosurie. De hiervoor | 440 | 349 | 594 | 145 | 131 |
| | | 125156 | Curve van verwekte hyper-of hypoglycemie (minimum vier doseringen), inclusief de eventuele doseringen van de glucosurie. De hiervoor gebruikte produ | 55220 | 63591 | 38549 | 28890 | 27805 |
| | insuline | 434210 | Doseren van insuline (Maximum 1) (Cumulregel 221, 322) Klasse 14 | 72398 | 103643 | 102985 | 104191 | 97807 |
| | | 546092 | Doseren van insuline (Maximum 1) (Cumulregel 221, 322) Klasse 14 | 8631 | 11912 | 12519 | 18037 | 27807 |
| full blood count | erythrocytes/hematocrite | 123034 | Tellen van de erythrocyten en/of hematocriet (Maximum 1) Klasse 2 | 6791 | 9527 | 7574 | 5394 | 4977 |
| | | 127035 | Tellen van de erythrocyten en/of hematocriet (Maximum 1) Klasse 2 | 3684831 | 4659025 | 4819885 | 5203039 | 5382568 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|---|---|---|
| | formula | 123071 | Leucocytenformule vastgesteld met microscoop op minimum 100 cellen (Maximum 1) (Cumulregel 100) Klasse 6 | 7347 | 9931 | 8283 | 6092 | 5642 |
| | | 123174 | Vereenvoudigde leucocytenformule (lymfocyten, monocyten en granulocyten), afgeleid van de analyse van een differentieel volumetrisch his | 6 | 47 | 66 | 26 | 28 |
| | | 123196 | Leucocytenformule ( ten minste vijf populaties), vastgesteld met cellenteller en gebaseerd op criteria die niet alleen de celgrootte omv | 7 | 74 | 13 | 14 | 6 |
| | | 127072 | Leucocytenformule vastgesteld met microscoop op minimum 100 cellen (Maximum 1) (Cumulregel 102) Klasse 6 | 359002 | 393617 | 378661 | 379692 | 309498 |
| | | 127175 | Vereenvoudigde leucocytenformule (lymfocyten, monocyten en granulocyten), afgeleid van de analyse van een differentieel volumetrisch histogram, verkrege | 11957 | 15531 | 13135 | 14575 | 14873 |
| | | 127190 | Leucocytenformule ( ten minste vijf populaties), vastgesteld met cellenteller en gebaseerd op criteria die niet alleen de celgrootte omvatten, inclusief | 2911123 | 3793516 | 3955865 | 4304227 | 4581611 |
| | hemoglobin | 123012 | Doseren van hemoglobine door elektrofotometrische methode (Maximum 1) Klasse 2 | 6134 | 8854 | 7057 | 5082 | 4778 |
| | | 127013 | Doseren van hemoglobine door elektrofotometrische methode (Maximum 1) Klasse 2 | 3642609 | 4703459 | 4840626 | 5205695 | 5398512 |
| | leucocytes | 123056 | Tellen van de leucocyten (Maximum 1) Klasse 2 | 7910 | 10673 | 8126 | 6529 | 6069 |
| | | 127050 | Tellen van de leucocyten (Maximum 1) Klasse 2 | 3616318 | 4651244 | 4790478 | 5150141 | 5349883 |
| | thrombocytes | 123115 | Tellen van de thrombocyten (Maximum 1) Klasse 2 | 3149 | 5196 | 3542 | 2210 | 2153 |
| | | 127116 | Tellen van de thrombocyten (Maximum 1) Klasse 2 | 3146797 | 4095000 | 4241348 | 4617453 | 4842635 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|---|---|---|
| hormonology | FSH | 434593 | Doseren van follikel stimulerend hormoon (FSH) (Maximum 1) (Cumulregel 309, 322) Klasse 14 | 177209 | 181306 | 140140 | 122120 | 78731 |
| | | 546136 | Doseren van follikelstimulerend hormoon (FSH) (Maximum 1) (Cumulregel 309, 322) Klasse 14 | 53341 | 103952 | 136151 | 167687 | 218131 |
| | LH | 434571 | Doseren van luteïniserend hormoon(LH) (Maximum 1) (Cumulregel 123, 322) Klasse 14 | 195178 | 194926 | 146732 | 131594 | 83324 |
| | | 546114 | Doseren van luteïniserend hormoon (LH) (Maximum 1) (Cumulregel 123, 322) Klasse 14 | 49899 | 101192 | 140968 | 170890 | 224882 |
| | Oestradiol | 434652 | Doseren van oestradiol (Maximum 1) (Cumulregel 212, 313, 322) Klasse 18 | 262377 | 285482 | 236943 | 212957 | 142813 |
| | | 546210 | Doseren van oestradiol (Maximum 1) (Cumulregel 212, 313, 322) Klasse 18 | 41761 | 89779 | 130845 | 174496 | 248819 |
| | Progest | 434674 | Doseren van progesteron (Maximum 1) (Cumulregel 314, 322) Klasse 17 | 232850 | 238914 | 186992 | 165117 | 114718 |
| | | 546232 | Doseren van progesteron (Maximum 1) (Cumulregel 314, 322) Klasse 17 | 34977 | 88426 | 129044 | 166408 | 219662 |
| | Prolactine | 434615 | Doseren van prolactine (Maximum 1) (Cumulregel 310, 322) Klasse 15 | 122459 | 123316 | 100147 | 83103 | 54228 |
| | | 546151 | Doseren van prolactine (Maximum 1) (Cumulregel 310, 322) Klasse 15 | 25487 | 59322 | 76252 | 98630 | 131250 |
| | Testosterone | 434895 | Doseren van testosteron (Maximum 1) (Cumulregel 322, 110) Klasse 17 | 86848 | 109533 | 108991 | 108960 | 108997 |
| | | 559613 | Doseren van testosteron (Maximum 1)(Cumulregel 110, 322) Klasse 17 | | | | | |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|---|---|---|
| inflammation | CRP | 541052 | Doseren van CRP met een immunologische methode (Maximum 1) (Cumulregel 35) Klasse 9 | 1615786 | 2272402 | 2468525 | 2828566 | 3079000 |
| | Fibrinogen | 554610 | Doseren van fibrinogeen (Maximum 1) (Cumulregel 101) Klasse 6 | 566564 | 688587 | 696669 | 756311 | 792855 |
| | sedimentation rate | 123152 | Meten van de snelheid van de globulaire sedimentatie (Maximum 1) Klasse 2 | 11706 | 16166 | 13714 | 9803 | 9065 |
| | | 127153 | Meten van de snelheid van de globulaire sedimentatie (Maximum 1) (Cumulregel 101) Klasse 2 | 2338395 | 2978692 | 3001582 | 3173040 | 3217078 |
| ions | Ca | 540190 | Doseren van calcium (Maximum 1) (Cumulregel 12) Klasse 6 | 1472074 | 1865913 | 1849208 | 2030554 | 2154612 |
| | Cl | 540256 | Doseren van chloriden (Maximum 1) Klasse 4 | 1587741 | 2075058 | 2068243 | 2259258 | 2412028 |
| | K | 540934 | Doseren van kalium (Maximum 1) Klasse 6 | 2144404 | 2823828 | 2870698 | 3131949 | 3327428 |
| | Mg | 540794 | Doseren van magnesium (Maximum 1) Klasse 7 | 642283 | 853519 | 857516 | 952468 | 1005781 |
| | Na | 541354 | Doseren van natrium (Maximum 1) Klasse 5 | 2018439 | 2653335 | 2693763 | 2952438 | 3141055 |
| | Na bicarbonates | 540492 | Doseren van de bicarbonaten in het plasma of het serum, met uitsluiting van de berekeningsresultaten die zijn verkregen uitgaande v | 808773 | 1083495 | 950758 | 992656 | 1075916 |
| kidney | creatinine | 540330 | Doseren van creatinine (Maximum 1) (Cumulregel 8) Klasse 5 | 3184090 | 4156578 | 4288373 | 4690870 | 4901199 |
| | Urea | 120072 | Doseren van ureum (Maximum 1) Klasse 3 | 4405 | 6077 | 4933 | 1985 | 1610 |
| | | 125075 | Doseren van ureum (Maximum 1) Klasse 3 | 2506826 | 3206639 | 3189919 | 3417827 | 3567300 |
| | Uric acid | 120013 | Doseren van urinezuur (Maximum 1) Klasse 4 | 4442 | 9135 | 5003 | 3160 | 2836 |
| | | 125016 | Doseren van urinezuur (Maximum 1) Klasse 4 | 2265976 | 2951084 | 2992990 | 3277567 | 3424607 |
| liver | Anti HCV | 551154 | Diagnose en controle van de evolutie van virale hepatitis C, door aantonen van anti-HC antilichamen (Maximum 1) (Cum | 105599 | 180078 | 215338 | 257194 | 282704 |
| | Anti-HAV | 551375 | Opsporen van specifieke IgG- of totale antilichamen tegen Hepatitis A (Maximum 1) (Cumulregel 328) Klasse 13 | 30143 | 61631 | 76899 | 98475 | 110451 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|---|---|---|
| | Anti-HBc | 437113 | Diagnose en controle van de evolutie van virale hepatitis B : door aantonen van HBc antilichaam (Cumulregel 234, 328) (Maximum 1) Klasse 13 | 42586 | 52386 | 44751 | 38419 | 22405 |
| | | 551471 | Diagnose en controle van de evolutie van virale hepatitis B door aantonen van anti HBc antilichamen met niet isotope | 80184 | 115661 | 124763 | 139434 | 156457 |
| | Anti-HBe | 437091 | Diagnose en controle van de evolutie van virale hepatitis B : door aantonen van HBe antilichaam (Cumulregel 233, 328) (Maximum 1) Klasse 13 | 3831 | 5543 | 4534 | 3890 | 2520 |
| | | 551456 | Diagnose en controle van de evolutie van virale hepatitis B door aantonen van anti HBe antilichamen met niet isotope | 7439 | 12634 | 16353 | 18394 | 20510 |
| | Anti-HBs | 437076 | Diagnose en controle van de evolutie van virale hepatitis B : door aantonen van HBs antilichaam (Cumulregel 232, 328) (Maximum 1) Klasse 13 | 49347 | 59675 | 46404 | 41520 | 29996 |
| | | 551434 | Diagnose en controle van de evolutie van virale hepatitis B door aantonen van anti HBs antilichamen met niet isotope | 102965 | 152929 | 176295 | 210487 | 236312 |
| | gamma GT | 541892 | Doseren van de gammaglutamyltransferasen (Maximum 1) (Cumulregel 23) Klasse 6 | 2669349 | 3526238 | 3591176 | 3928328 | 4125097 |
| | GOT, ASAT | 120094 | Doseren van aspartaat aminotransferasen (Maximum 1) (Cumulregel 2) Klasse 6 | 481 | 496 | 431 | 315 | 9 |
| | | 125090 | Doseren van aspartaat aminotransferasen (Maximum 1) (Cumulregel 4) Klasse 6 | 104025 | 132604 | 141770 | 153556 | 187810 |
| | GOT,ASAT & GPT, ALAT | 120131 | Doseren van aspartaat aminotransferasen en alanine aminotransferasen (Maximum 1) (Cumulregel 2) Klasse 10 | 4526 | 6071 | 4913 | 3065 | 2992 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|---|---|---|
| | | 125134 | Doseren van aspartaat aminotransferasen en alanine aminotransferasen (Maximum 1) (Cumulregel 4) Klasse 10 | 2662655 | 3446608 | 3523777 | 3815096 | 3948699 |
| | GPT, ALAT | 120116 | Doseren van alanine aminotransferasen (Maximum 1) (Cumulregel 2) Klasse 6 | 463 | 492 | 424 | 309 | 6 |
| | | 125112 | Doseren van alanine aminotransferasen (Maximum 1) (Cumulregel 4) Klasse 6 | 105681 | 158569 | 192075 | 249749 | 286998 |
| | HBe Ag | 437054 | Diagnose en controle van de evolutie van virale hepatitis B : door aantonen van HBe antigeen (Cumulregel 231, 328) (Maximum 1) Klasse 13 | 4673 | 5613 | 4593 | 4136 | 2698 |
| | | 551412 | Diagnose en controle van de evolutie van virale hepatitis B door aantonen van HBe antigeen met niet isotopenmethode | 8751 | 14109 | 17235 | 20196 | 22222 |
| | HBs Ag | 437032 | Diagnose en controle van de evolutie van virale hepatitis B : door aantonen van HBs antigeen (Maximum 1)(Cumulregel 230, 328) Klasse 13 | 85627 | 93653 | 69418 | 60185 | 43175 |
| | | 551390 | Diagnose en controle van de evolutie van virale hepatitis B door aantonen van HBs antigeen met niet isotopenmethode | 190859 | 278049 | 310967 | 339688 | 362507 |
| | IgM anti-HAV | 437010 | Aantonen van recente infectie door hepati | 13415 | 15027 | 10954 | 9670 | 7027 |
| | | 551353 | Diagnose van een recente hepatitis A virus-infectie door opzoeken van IgM antilichamen met niet isotopenmethode (Ma | 69274 | 99410 | 100333 | 112193 | 117134 |
| | LDH | 541774 | Doseren van melkzuurdehydrogenasen (Maximum 1) (Cumulregel 10) Klasse 6 | 1470695 | 1938338 | 1952711 | 2130860 | 2167443 |
| | Phos alc | 541914 | Doseren van de alkalische fosfatasen (Maximum 1) Klasse 6 | 2240793 | 2910448 | 2909473 | 3140540 | 3274465 |
| | T-BIL/D-BIL | 120035 | Doseren van bilirubine (Maximum 1) Klasse 5 | 4052 | 5531 | 4419 | 2787 | 2633 |
| | | 125031 | Doseren van bilirubine (Maximum 1) (Cumulregel 5) Klasse 5 | 327686 | 421980 | 415890 | 445739 | 485987 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|---|---|---|
| | | 540175 | Doseren van totale bilirubine en van de fracties ervan (Maximum 1) (Cumulregel 5) Klasse 8 | 1136638 | 1493791 | 1488075 | 1622609 | 1679565 |
| pancreas | amylase | 541612 | Doseren van amylasen (Maximum 1) (Cumulregel 21) Klasse 9 | 827405 | 1113633 | 1110160 | 1231239 | 1301843 |
| | lipase | 541833 | Doseren van lipasen (Maximum 1) Klasse 9 | 607691 | 840850 | 856853 | 971633 | 1041128 |
| protein | electro | 540455 | Electroforese van proteïnen met curve en berekening (Maximum 1) (Cumulregel 11) Klasse 12 | 1010955 | 1291586 | 1234778 | 1288516 | 1297029 |
| | protein tot | 125532 | Doseren van totale proteïnen (Maximum 1) (Diagnoseregel 1) Klasse 3 | 158429 | 204902 | 207808 | 227989 | 239894 |
| | | 540956 | Doseren van totale proteïnen (Maximum 1) Klasse 3 | 1650632 | 2127453 | 2089605 | 2221351 | 2297942 |
| rheumatism | Waaler Rose | 124530 | Test van Waaler Rose op plaatje (Maximum 1) Klasse 3 | 2102 | 2420 | 2166 | 2202 | 2074 |
| | | 128531 | Test van Waaler Rose op plaatje (Maximum 1) (Cumulregel 109) Klasse 3 | 33483 | 39128 | 22958 | 18703 | 17402 |
| thyriod | Antimicrosomial antibodies | 438056 | Doseren van thyroperoxydase antilichamen (anti-TPO) (Maximum 1) (Cumulregel 330) Klasse 13 | 104227 | 141147 | 145019 | 159872 | 165104 |
| | | 556091 | Opzoeken en titreren van anti-thyroied microsomen of anti-thyroperoxidase antilichamen (Maximum 1) | 43547 | 62574 | 62701 | 72141 | 78065 |
| | Antithyroglobul antibodies | 438071 | Doseren van thyroglobuline antilichamen (Maximum 1) (Cumulregel 331) Klasse 13 | 103957 | 139962 | 143955 | 157089 | 161170 |
| | | 556076 | Opzoeken en titreren van antithyroglobuline-antilichamen (Maximum 1) (Cumulregel 331) Klasse 13 | 44010 | 63198 | 62728 | 71617 | 77074 |
| | T3 free | 434394 | Doseren van vrije T3 (Maximum 1) (Cumulregel 218, 220) Klasse 15 | 201234 | 264982 | 234987 | 233025 | 162302 |
| | | 546291 | Doseren van vrije T3 (Maximum 1)(Cumulregel 218, 220) Klasse 15 | | | 50941 | 137500 | 271463 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|---|---|---|
| | T3 total | 435013 | Doseren van totale triiodothyoronine (T3) of van thyroxine bindend globuline (TBG) of de saturatiecapaciteit van thyroxine bindend globuline | | | 197 | 5772 | 11081 |
| | | 559252 | Doseren van totaal trilodothyronine (T3) en van thyroxine bindend globuline (TBG) of van de saturatiecapaciteit van | | | | | |
| | T4 free | 434335 | Doseren van vrije T4 (Maximum 1) (Cumulregel 218, 219) Klasse 15 | 478384 | 733778 | 663792 | 600464 | 463267 |
| | | 546276 | Doseren van vrije T4 (Maximum 1)(Cumulregel 218, 219) Klasse 15 | | | 205312 | 528096 | 849397 |
| | T4 total | 434991 | Doseren van totale thyroxine (T4) en van het thyroxine bindend globuline (TBG) of de saturatiecapaciteit van thyroxine bindend globuline (Maximum 1)15 | | | 8639 | 12720 | 12442 |
| | | 546070 | Doseren van totale thyroxine (T4) en van het thyroxine bindend globuline (TBG) of de saturatiecapaciteit van thyroxi | 245066 | 337584 | 247508 | 197417 | 172157 |
| | Thyroglobul. | 434291 | Doseren van thyroglobuline (Maximum 1) (cumulregel 94) Klasse 14 | 106379 | 145022 | 146190 | 160521 | 166308 |
| | | 559230 | Doseren van thyroglobuline (Maximum 1)(Cumulregel 94) Klasse 14 | | | | | |
| | TSH | 434313 | Doseren van schildklier-stimulerend hormoon (TSH) (Maximum 1) (Cumulregel 218, 311, 322) Klasse 13 | 1003944 | 1256421 | 1206806 | 1107208 | 784888 |
| | | 546173 | Doseren van schildklier stimulerend hormoon (TSH) (Maximum 1) (Cumulregel 218, 311, 322) Klasse 13 | 501050 | 892273 | 1075212 | 1521514 | 2017652 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| tumour markers | C.E.A. | 436192 | Therapeutische Monitoring 1/Bloed : Doseren van C E A (Maximum 1 | 66134 | 70823 | 51491 | 47014 | 33573 |
| | | 548332 | Therapeutische Monitoring 1/Bloed : Doseren van C E A met niet isotopenmethode (Maximum 1) (Cumulregel 201, 317) (Diagnoseregel 46) Klasse | 28048 | 49030 | 67382 | 81271 | 105044 |
| | CA 15.3 | 436170 | Therapeutische Monitoring 1/Bloed : Doseren van CA 15 3 (Maximum | 42905 | 50524 | 45051 | 46667 | 37633 |
| | | 548310 | Therapeutische Monitoring 1/Bloed : Doseren van CA 15 3 met niet isotopenmethode (Maximum 1) (Cumulregel 201, 315) (Diagnoseregel 46) Klass | 14996 | 24469 | 33637 | 45490 | 70313 |
| | CA 19-10 | 548354 | Therapeutische Monitoring 1/Bloed : Doseren van carbohydrate antigen 19-9 (CA 19-9) (Maximum 1)(Cumulregel 201)(Diagnoseregel 46) Klasse 20 | 3022 | 5660 | 7898 | 10771 | 14415 |
| | CA 19-9 | 436214 | Therapeutische Monitoring 1/Bloed : Doseren van carbohydrate ant | 9671 | 12433 | 12456 | 12987 | 11055 |

**Table 1. RIZIV/INAMI use of selected laboratory tests per nomenclature number between 2000 and 2005**

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| allergy | RAST | 438115 | Bepalen van specifieke IgE per antigeen (Maximum 6) (Cumulregel 47) Klasse 13 | 549094 | 430733 | 271538 | 205337 | 197157 | 155488 |
| | | 556275 | Bepalen van specifieke IgE per antigeen (Maximum 6)(Cumulregel 47) Klasse 13 | 710572 | 810912 | 972705 | 984713 | 1092533 | 1174353 |
| | total IgE | 438093 | Doseren van IgE totaal (Maximum 1) (Cumulregel 46) Klasse 13 | 120341 | 108937 | 66198 | 39222 | 36902 | 29940 |
| | | 556253 | Doseren van IgE totaal (Maximum 1)(Cumulregel 46) Klasse 13 | 272565 | 298132 | 343075 | 368604 | 400519 | 408245 |
| anemia | ferritin | 433090 | Doseren van ferritine (Maximum 1) (Cumulregel 305) Klass | 362002 | 204345 | 149767 | 135327 | 87804 | 77030 |
| | | 541472 | Doseren van ferritine met niet isotopenmethode (Maximum 1) (Cumulregel 305) Klasse 13 | 1920518 | 2300939 | 2416480 | 2636749 | 2921687 | 3095087 |
| | Folic acid | 433053 | Doseren van foliumzuur in het serum (Maximum 1) (Cumulregel 303) Klasse 13 | 19016 | 17407 | 17533 | 10893 | 8747 | 6694 |
| | | 541435 | Doseren van foliumzuur in het serum met niet isotopenmethode (Maximum 1) (Cumulregel 303) Klasse 13 | 29173 | 37190 | 47350 | 69857 | 73994 | 68963 |
| | Folic acid eryhtrocytes | 433075 | Doseren van foliumzuur in de erythrocyten (Maximum 1) (C | 58600 | 55907 | 47740 | 39971 | 32862 | 16916 |
| | | 541450 | Doseren van foliumzuur in de erythrocyten met niet isotopenmethode (Maximum 1) (Cumulregel 304) Klasse 14 | 65564 | 82722 | 95087 | 122552 | 144328 | 173020 |
| | Iron | 540551 | Doseren van ijzer (Maximum 1) (Cumulregel 15) Klasse 9 | 2366701 | 2570792 | 2588627 | 2702214 | 2876306 | 2959291 |
| | Iron & RBC | 540573 | Doseren van ijzer en bepalen van het ijzerbindend vermogen (Maximum 1) (Cumulregel 15, 16) Klasse 11 | 590622 | 554423 | 507883 | 541380 | 542017 | 549910 |
| | transferrin | 541030 | Doseren van transferrine met een immunologische methode (Maximum 1) (Cumulregel 16) Klasse 9 | 693172 | 761687 | 770094 | 811665 | 885639 | 938161 |
| | Vit B12 | 433112 | Doseren van vitamine B12 (Maximum 1) (Cumulregel 303) Klasse 13 | 53273 | 52759 | 36957 | 32684 | 23705 | 16139 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| | | 541494 | Doseren van vitamine B12 met niet isotopenmethode (Maximum 1) (Cumulregel 303) Klasse 13 | 103408 | 129618 | 168128 | 220868 | 238810 | 266253 |
| | Vit B12 & folic acid | 433134 | Doseren van vitamine B12 en foliumzuur (Maximum 1) (Cumulregel 303) Klasse 16 | 216932 | 191840 | 127913 | 103598 | 82989 | 58721 |
| | | 541391 | Doseren van vitamine B12 en foliumzuur, met niet isotopenmethode (Maximum 1) (Cumulregel 303) Klasse 16 | 418859 | 520387 | 592001 | 704364 | 865409 | 988855 |
| cardiovascular | HDL-cholesterol | 540293 | Doseren van HDL-cholesterol (Maximum 1) (Cumulregel 13) Klasse 10 | 3426357 | 3567735 | 3544286 | 3711124 | 3966389 | 4042358 |
| | LDL-cholesterol | 542231 | Doseren van LDL-cholesterol, met uitsluiting van berekeningsmethoden (Maximum 1)(Cumulregel 13) (Diagnoseregel 54) Klasse 14 | 97641 | 164158 | 184928 | 207370 | 230141 | 256567 |
| | Total cholesterolerol | 540271 | Doseren van totale cholesterol (Maximum 1) Klasse 6 | 3942344 | 4139771 | 4121760 | 4280527 | 4534774 | 4602884 |
| | triglycerides | 541376 | Doseren van triglyceriden (Maximum 1) Klasse 8 | 3719043 | 3917669 | 3899264 | 4061911 | 4318479 | 4398941 |
| coagulation | INR/Quick | 554573 | Thromboplastinetijd (prothrombinetijd) (Maximum 1) (Cumulregel 54) Klasse 6 | 2265464 | 2445159 | 2560582 | 2765646 | 2987549 | 3088030 |
| | PTT | 554676 | Geactiveerde gedeeltelijke thromboplastinetijd (Maximum 1)(Cumulregel 107) Klasse 8 | 680145 | 719260 | 736907 | 793191 | 861735 | 884215 |
| diabetes | C-peptide | 434173 | Doseren van C-peptide (Maximum 1) (Cumulregel 322, 89) Klasse 16 | 52771 | 58512 | 51419 | 48791 | 45213 | 34830 |
| | | 559134 | Doseren van C-peptide (Maximum 1)(Cumulregel 89, 322) Klasse 16 | | 541 | 11866 | 20722 | 32894 | 46221 |
| | glucose | 120050 | Doseren van glucose (Maximum 1) (Cumulregel 1) Klasse 3 | 3799 | 1546 | 1112 | 753 | 701 | 623 |
| | | 125053 | Doseren van glucose (Maximum 1) (Cumulregel 3) Klasse 3 | 4599089 | 4852351 | 4880115 | 5150370 | 5448918 | 5569786 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| | Glucose (+4) | 120190 | Glucosedagcurve (minimum 4 doseringen), inclusief de eventuele doseringen van de glucosurie (Maximum 1)(Cumulregel 1) Klasse 18 | 58 | 39 | 33 | 20 | 28 | 24 |
| | | 125193 | Glucosedagcurve (minimum 4 doseringen), inclusief de eventuele doseringen van de glucosurie (Maximum 1)(Cumulregel 3) Klasse 18 | 22231 | 20361 | 19788 | 18329 | 17159 | 23110 |
| | Hb gly | 540750 | Doseren van glycohemoglobine in hemolysaat (Maximum 1) (Cumulregel 18) (Diagnoseregel 56) Klasse 13 | 841231 | 908179 | 941303 | 1025536 | 1142756 | 1204493 |
| | Hyperglycemia curve | 120153 | Curve van verwekte hyper- of hypoglycemie (minimum vier doseringen), inclusief de eventuele doseringen van de glucosurie. De hiervoor | 66 | 25 | 14 | 8 | 5 | 4 |
| | | 125156 | Curve van verwekte hyper-of hypoglycemie (minimum vier doseringen), inclusief de eventuele doseringen van de glucosurie. De hiervoor gebruikte produ | 27665 | 26386 | 25821 | 27595 | 37020 | 46374 |
| | insuline | 434210 | Doseren van insuline (Maximum 1) (Cumulregel 221, 322) Klasse 14 | 95488 | 91723 | 77074 | 62214 | 65146 | 47680 |
| | | 546092 | Doseren van insuline (Maximum 1) (Cumulregel 221, 322) Klasse 14 | 37269 | 54457 | 81174 | 110443 | 129948 | 161189 |
| full blood count | erythrocytes/hematocrite | 123034 | Tellen van de erythrocyten en/of hematocriet (Maximum 1) Klasse 2 | 4507 | 3347 | 2625 | 2237 | 2109 | 2085 |
| | | 127035 | Tellen van de erythrocyten en/of hematocriet (Maximum 1) Klasse 2 | 5673504 | 5968328 | 6049801 | 6317696 | 6641939 | 6814930 |
| | formula | 123071 | Leucocytenformule vastgesteld met microscoop op minimum 100 cellen (Maximum 1) (Cumulregel 100) Klasse 6 | 5429 | 4150 | 3533 | 3124 | 2908 | 2839 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| | | 123174 | Vereenvoudigde leucocytenformule (lymfocyten, monocyten en granulocyten), afgeleid van de analyse van een differentieel volumetrisch his | 21 | 19 | 8 | 16 | 12 | 12 |
| | | 123196 | Leucocytenformule ( ten minste vijf populaties), vastgesteld met cellenteller en gebaseerd op criteria die niet alleen de celgrootte omv | 4 | 25 | 3 | | 1 | |
| | | 127072 | Leucocytenformule vastgesteld met microscoop op minimum 100 cellen (Maximum 1) (Cumulregel 102) Klasse 6 | 287328 | 290462 | 143854 | 148794 | 142047 | 137585 |
| | | 127175 | Vereenvoudigde leucocytenformule (lymfocyten, monocyten en granulocyten), afgeleid van de analyse van een differentieel volumetrisch histogram, verkrege | 16355 | 13092 | 8747 | 8007 | 6300 | 5733 |
| | | 127190 | Leucocytenformule ( ten minste vijf populaties), vastgesteld met cellenteller en gebaseerd op criteria die niet alleen de celgrootte omvatten, inclusief | 4899966 | 5203880 | 5407854 | 5669173 | 5966688 | 6147467 |
| | hemoglobin | 123012 | Doseren van hemoglobine door elektrofotometrische methode (Maximum 1) Klasse 2 | 4210 | 3097 | 2492 | 1909 | 1793 | 1872 |
| | | 127013 | Doseren van hemoglobine door elektrofotometrische methode (Maximum 1) Klasse 2 | 5695957 | 6008818 | 6098870 | 6372063 | 6702097 | 6881197 |
| | leucocytes | 123056 | Tellen van de leucocyten (Maximum 1) Klasse 2 | 5822 | 4420 | 3785 | 3316 | 3109 | 3036 |
| | | 127050 | Tellen van de leucocyten (Maximum 1) Klasse 2 | 5631723 | 5933566 | 6025082 | 6290280 | 6606276 | 6783519 |
| | thrombocytes | 123115 | Tellen van de thrombocyten (Maximum 1) Klasse 2 | 1903 | 1331 | 1235 | 961 | 1073 | 1148 |
| | | 127116 | Tellen van de thrombocyten (Maximum 1) Klasse 2 | 5146383 | 5452003 | 5534200 | 5819678 | 6146982 | 6329402 |
| hormonology | FSH | 434593 | Doseren van follikel stimulerend hormoon (FSH) (Maximum 1) (Cumulregel 309, 322) Klasse 14 | 45739 | 39632 | 30411 | 25104 | 21144 | 15489 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| | | 546136 | Doseren van follikelstimulerend hormoon (FSH) (Maximum 1) (Cumulregel 309, 322) Klasse 14 | 266901 | 292958 | 307626 | 323118 | 346853 | 358186 |
| | LH | 434571 | Doseren van luteïniserend hormoon(LH) (Maximum 1) (Cumulregel 123, 322) Klasse 14 | 47405 | 40195 | 28306 | 20649 | 20018 | 14211 |
| | | 546114 | Doseren van luteïniserend hormoon (LH) (Maximum 1) (Cumulregel 123, 322) Klasse 14 | 271788 | 293528 | 320737 | 341800 | 364222 | 376792 |
| | Oestradiol | 434652 | Doseren van oestradiol (Maximum 1) (Cumulregel 212, 313, 322) Klasse 18 | 81845 | 74903 | 53796 | 37857 | 33374 | 22021 |
| | | 546210 | Doseren van oestradiol (Maximum 1) (Cumulregel 212, 313, 322) Klasse 18 | 318995 | 339865 | 370649 | 385092 | 415412 | 428843 |
| | Progest | 434674 | Doseren van progesteron (Maximum 1) (Cumulregel 314, 322) Klasse 17 | 63782 | 55451 | 36379 | 23334 | 17797 | 12955 |
| | | 546232 | Doseren van progesteron (Maximum 1) (Cumulregel 314, 322) Klasse 17 | 280795 | 302550 | 320768 | 348097 | 383879 | 394246 |
| | Prolactine | 434615 | Doseren van prolactine (Maximum 1) (Cumulregel 310, 322) Klasse 15 | 38978 | 35506 | 29834 | 25550 | 25788 | 19322 |
| | | 546151 | Doseren van prolactine (Maximum 1) (Cumulregel 310, 322) Klasse 15 | 157041 | 171268 | 180078 | 191582 | 201357 | 213402 |
| | Testosterone | 434895 | Doseren van testosteron (Maximum 1) (Cumulregel 322, 110) Klasse 17 | 113078 | 123571 | 93401 | 88512 | 81317 | 69031 |
| | | 559613 | Doseren van testosteron (Maximum 1)(Cumulregel 110, 322) Klasse 17 | | 2287 | 43819 | 56138 | 70114 | 82439 |
| inflammation | CRP | 541052 | Doseren van CRP met een immunologische methode (Maximum 1) (Cumulregel 35) Klasse 9 | 3419019 | 3771016 | 3930213 | 4242071 | 4620121 | 4910970 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| | Fibrinogen | 554610 | Doseren van fibrinogeen (Maximum 1) (Cumulregel 101) Klasse 6 | 827070 | 881981 | 875798 | 918502 | 970940 | 960432 |
| | sedimentation rate | 123152 | Meten van de snelheid van de globulaire sedimentatie (Maximum 1) Klasse 2 | 8077 | 6198 | 5113 | 4264 | 3320 | 3058 |
| | | 127153 | Meten van de snelheid van de globulaire sedimentatie (Maximum 1) (Cumulregel 101) Klasse 2 | 3298103 | 3398906 | 3367965 | 3433027 | 3509080 | 3550254 |
| ions | Ca | 540190 | Doseren van calcium (Maximum 1) (Cumulregel 12) Klasse 6 | 2346723 | 2485917 | 2474818 | 2630120 | 2817024 | 2917295 |
| | Cl | 540256 | Doseren van chloriden (Maximum 1) Klasse 4 | 2636634 | 2851216 | 2905522 | 3132820 | 3403632 | 3534723 |
| | K | 540934 | Doseren van kalium (Maximum 1) Klasse 6 | 3612982 | 3899179 | 3993568 | 4278617 | 4609500 | 4782786 |
| | Mg | 540794 | Doseren van magnesium (Maximum 1) Klasse 7 | 1085854 | 1176015 | 1172544 | 1261286 | 1356911 | 1403553 |
| | Na | 541354 | Doseren van natrium (Maximum 1) Klasse 5 | 3425093 | 3710658 | 3811982 | 4100302 | 4423526 | 4601122 |
| | Na bicarbonates | 540492 | Doseren van de bicarbonaten in het plasma of het serum, met uitsluiting van de berekeningsresultaten die zijn verkregen uitgaande v | 1209566 | 1320199 | 1348453 | 1487001 | 1665579 | 1776036 |
| kidney | creatinine | 540330 | Doseren van creatinine (Maximum 1) (Cumulregel 8) Klasse 5 | 5233148 | 5565471 | 5678032 | 5977858 | 6322207 | 6505678 |
| | U-albumin | 433554 | Doseren van albumine in micro-hoeveelheid, door een immunologische methode (Maximum 1)(cumulregel 69)(Diagnoseregel 3) Klasse 10 | 194 | 267 | | | 1 | |
| | | 543712 | Doseren van albumine in micro-hoeveelheid door een immunologische methode (Maximum 1)(Cumulregel 69) (Diagnoseregel 3) Klasse 10 | 77117 | 87243 | 103372 | 119010 | 134582 | 145638 |
| | U-creat | 543255 | Doseren van creatinine (Maximum 1) (Cumulregel 8) Klasse 6 | 92383 | 98903 | 106936 | 118130 | 134939 | 148675 |
| | Urea | 120072 | Doseren van ureum (Maximum 1) Klasse 3 | 995 | 391 | 363 | 312 | 422 | 419 |
| | | 125075 | Doseren van ureum (Maximum 1) Klasse 3 | 3810933 | 4090435 | 4138814 | 4395245 | 4691065 | 4843304 |
| | Uric acid | 120013 | Doseren van urinezuur (Maximum 1) Klasse 4 | 2271 | 948 | 605 | 439 | 428 | 417 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| | | 125016 | Doseren van urinezuur (Maximum 1) Klasse 4 | 3665887 | 3922383 | 3940315 | 4127399 | 4342705 | 4446676 |
| liver | Anti HCV | 551154 | Diagnose en controle van de evolutie van virale hepatitis C, door aantonen van anti-HC antilichamen (Maximum 1) (Cum | 342386 | 377480 | 397148 | 436621 | 521785 | 517643 |
| | Anti-HAV | 551375 | Opsporen van specifieke IgG- of totale antilichamen tegen Hepatitis A (Maximum 1) (Cumulregel 328) Klasse 13 | 128958 | 142441 | 144047 | 155979 | 194105 | 196469 |
| | Anti-HBc | 437113 | Diagnose en controle van de evolutie van virale hepatitis B : door aantonen van HBc antilichaam (Cumulregel 234, 328) (Maximum 1) Klasse 13 | 12530 | 9918 | 3966 | 2817 | 2165 | 2036 |
| | | 551471 | Diagnose en controle van de evolutie van virale hepatitis B door aantonen van anti HBc antilichamen met niet isotope | 183715 | 195411 | 197819 | 208485 | 232372 | 229335 |
| | Anti-HBe | 437091 | Diagnose en controle van de evolutie van virale hepatitis B : door aantonen van HBe antilichaam (Cumulregel 233, 328) (Maximum 1) Klasse 13 | 2082 | 1746 | 1006 | 743 | 652 | 649 |
| | | 551456 | Diagnose en controle van de evolutie van virale hepatitis B door aantonen van anti HBe antilichamen met niet isotope | 22732 | 24056 | 24321 | 25096 | 27904 | 25652 |
| | Anti-HBs | 437076 | Diagnose en controle van de evolutie van virale hepatitis B : door aantonen van HBs antilichaam (Cumulregel 232, 328) (Maximum 1) Klasse 13 | 17636 | 10542 | 6407 | 4735 | 3678 | 3777 |
| | | 551434 | Diagnose en controle van de evolutie van virale hepatitis B door aantonen van anti HBs antilichamen met niet isotope | 279218 | 305343 | 308546 | 325738 | 380647 | 387927 |
| | gamma GT | 541892 | Doseren van de gammaglutamyltransferasen (Maximum 1) (Cumulregel 23) Klasse 6 | 4402711 | 4691199 | 4765849 | 5023839 | 5338027 | 5502741 |
| | GOT, ASAT | 120094 | Doseren van aspartaat aminotransferasen (Maximum 1) (Cumulregel 2) Klasse 6 | 2 | 8 | 12 | 6 | 5 | 4 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| | | 125090 | Doseren van aspartaat aminotransferasen (Maximum 1) (Cumulregel 4) Klasse 6 | 175089 | 177010 | 179598 | 159344 | 118973 | 163754 |
| | GOT,ASAT & GPT, ALAT | 120131 | Doseren van aspartaat aminotransferasen en alanine aminotransferasen (Maximum 1) (Cumulregel 2) Klasse 10 | 2409 | 893 | 818 | 603 | 679 | 599 |
| | | 125134 | Doseren van aspartaat aminotransferasen en alanine aminotransferasen (Maximum 1) (Cumulregel 4) Klasse 10 | 4202314 | 4475418 | 4524035 | 4795063 | 5131369 | 5245650 |
| | GPT, ALAT | 120116 | Doseren van alanine aminotransferasen (Maximum 1) (Cumulregel 2) Klasse 6 | 3 | 2 | 2 | 4 | 2 | 1 |
| | | 125112 | Doseren van alanine aminotransferasen (Maximum 1) (Cumulregel 4) Klasse 6 | 291070 | 299085 | 366478 | 335577 | 318305 | 337575 |
| | HBe Ag | 437054 | Diagnose en controle van de evolutie van virale hepatitis B : door aantonen van HBe antigeen (Cumulregel 231, 328) (Maximum 1) Klasse 13 | 2134 | 1341 | 1033 | 749 | 588 | 650 |
| | | 551412 | Diagnose en controle van de evolutie van virale hepatitis B door aantonen van HBe antigeen met niet isotopenmethode | 25940 | 28151 | 29318 | 31131 | 35349 | 33755 |
| | HBs Ag | 437032 | Diagnose en controle van de evolutie van virale hepatitis B : door aantonen van HBs antigeen (Maximum 1)(Cumulregel 230, 328) Klasse 13 | 25268 | 17854 | 8249 | 5899 | 4189 | 3910 |
| | | 551390 | Diagnose en controle van de evolutie van virale hepatitis B door aantonen van HBs antigeen met niet isotopenmethode | 412837 | 433978 | 444068 | 470686 | 523988 | 520528 |
| | IgM anti-HAV | 437010 | Aantonen van recente infectie door hepati | 5811 | 5513 | 3100 | 2902 | 4062 | 1969 |
| | | 551353 | Diagnose van een recente hepatitis A virus-infectie door opzoeken van IgM antilichamen met niet isotopenmethode (Ma | 126297 | 130495 | 124492 | 126964 | 149390 | 146335 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| | LDH | 541774 | Doseren van melkzuurdehydrogenasen (Maximum 1) (Cumulregel 10) Klasse 6 | 2268994 | 2415285 | 2307331 | 2490286 | 2679342 | 2767364 |
| | Phos alc | 541914 | Doseren van de alkalische fosfatasen (Maximum 1) Klasse 6 | 3498285 | 3688254 | 3645324 | 3825918 | 4053695 | 4153997 |
| | T-BIL/D-BIL | 120035 | Doseren van bilirubine (Maximum 1) Klasse 5 | 2230 | 988 | 616 | 485 | 428 | 376 |
| | | 125031 | Doseren van bilirubine (Maximum 1) (Cumulregel 5) Klasse 5 | 539863 | 565295 | 554860 | 563120 | 584320 | 589026 |
| | | 540175 | Doseren van totale bilirubine en van de fracties ervan (Maximum 1) (Cumulregel 5) Klasse 8 | 1801752 | 1949777 | 1950804 | 2101719 | 2268990 | 2345965 |
| pancreas | amylase | 541612 | Doseren van amylasen (Maximum 1) (Cumulregel 21) Klasse 9 | 1424516 | 1518364 | 1499711 | 1637857 | 1774775 | 1828916 |
| | lipase | 541833 | Doseren van lipasen (Maximum 1) Klasse 9 | 1161852 | 1269635 | 1269057 | 1400598 | 1537620 | 1598131 |
| protein | electro | 540455 | Electroforese van proteïnen met curve en berekening (Maximum 1) (Cumulregel 11) Klasse 12 | 1359447 | 1410606 | 1329704 | 1371870 | 1411726 | 1423833 |
| | protein tot | 125532 | Doseren van totale proteïnen (Maximum 1) (Diagnoseregel 1) Klasse 3 | 241167 | 252282 | 237854 | 246840 | 270125 | 289070 |
| | | 540956 | Doseren van totale proteïnen (Maximum 1) Klasse 3 | 2459640 | 2598877 | 2558211 | 2661816 | 2785278 | 2824683 |
| rheumatism | Waaler Rose | 124530 | Test van Waaler Rose op plaatje (Maximum 1) Klasse 3 | 1560 | 238 | 211 | 169 | 134 | 104 |
| | | 128531 | Test van Waaler Rose op plaatje (Maximum 1) (Cumulregel 109) Klasse 3 | 13277 | 8334 | 8375 | 7531 | 5780 | 6083 |
| thyriod | Antimicrosomial antibodies | 438056 | Doseren van thyroperoxydase antilichamen (anti-TPO) (Maximum 1) (Cumulregel 330) Klasse 13 | 178887 | 191426 | 151897 | 134240 | 111209 | 89157 |
| | | 556091 | Opzoeken en titreren van anti-thyroied microsomen of anti-thyroperoxidase antilichamen (Maximum 1) | 87781 | 97734 | 140836 | 182904 | 240266 | 274721 |
| | Antithyroglobul antibodies | 438071 | Doseren van thyroglobuline antilichamen (Maximum 1) (Cumulregel 331) Klasse 13 | 172407 | 180826 | 145547 | 126449 | 108693 | 86735 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| | | 556076 | Opzoeken en titreren van antithyroglobuline-antilichamen (Maximum 1) (Cumulregel 331) Klasse 13 | 87994 | 98622 | 137540 | 176958 | 227440 | 263226 |
| | T3 free | 434394 | Doseren van vrije T3 (Maximum 1) (Cumulregel 218, 220) Klasse 15 | 146315 | 130698 | 96895 | 70754 | 65340 | 72035 |
| | | 546291 | Doseren van vrije T3 (Maximum 1)(Cumulregel 218, 220) Klasse 15 | 355375 | 426597 | 502658 | 582985 | 658776 | 687482 |
| | T3 total | 435013 | Doseren van totale triiodothyoronine (T3) of van thyroxine bindend globuline (TBG) of de saturatiecapaciteit van thyroxine bindend globuline | 12172 | 12997 | 4530 | 5218 | 4554 | 1849 |
| | | 559252 | Doseren van totaal trilodothyronine (T3) en van thyroxine bindend globuline (TBG) of van de saturatiecapaciteit van | | 2289 | 31820 | 32477 | 29431 | 29541 |
| | T4 free | 434335 | Doseren van vrije T4 (Maximum 1) (Cumulregel 218, 219) Klasse 15 | 353270 | 301262 | 208740 | 138806 | 132948 | 124275 |
| | | 546276 | Doseren van vrije T4 (Maximum 1)(Cumulregel 218, 219) Klasse 15 | 1165004 | 1427323 | 1605887 | 1837421 | 2081102 | 2213628 |
| | T4 total | 434991 | Doseren van totale thyroxine (T4) en van het thyroxine bindend globuline (TBG) of de saturatiecapaciteit van thyroxine bindend globuline (Maximum 1)15 | 4 | 780 | 11727 | 12138 | 12181 | 3654 |
| | | 546070 | Doseren van totale thyroxine (T4) en van het thyroxine bindend globuline (TBG) of de saturatiecapaciteit van thyroxi | 159162 | 138347 | 117624 | 104339 | 55728 | 47178 |
| | Thyroglobul. | 434291 | Doseren van thyroglobuline (Maximum 1) (cumulregel 94) Klasse 14 | 180537 | 192847 | 148022 | 130742 | 122947 | 99268 |
| | | 559230 | Doseren van thyroglobuline (Maximum 1)(Cumulregel 94) Klasse 14 | | 3296 | 57466 | 86172 | 114216 | 144504 |
| | TSH | 434313 | Doseren van schildklier-stimulerend hormoon (TSH) (Maximum 1) (Cumulregel 218, 311, 322) Klasse 13 | 522957 | 378230 | 186846 | 135802 | 132693 | 124327 |

| Cluster | Subcluster | Nomen-clature | Label (dutch) | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|---|---|---|---|---|
| | | 546173 | Doseren van schildklier stimulerend hormoon (TSH) (Maximum 1) (Cumulregel 218, 311, 322) Klasse 13 | 2549979 | 2966528 | 3236900 | 3497742 | 3727412 | 3839880 |
| tumour markers | C.E.A. | 436192 | Therapeutische Monitoring 1/Bloed : Doseren van C E A (Maximum 1 | 25275 | 19991 | 13159 | 9569 | 7817 | 5535 |
| | | 548332 | Therapeutische Monitoring 1/Bloed : Doseren van C E A met niet isotopenmethode (Maximum 1) (Cumulregel 201, 317) (Diagnoseregel 46) Klasse | 130238 | 146509 | 159777 | 179619 | 194745 | 212894 |
| | CA 15.3 | 436170 | Therapeutische Monitoring 1/Bloed : Doseren van CA 15 3 (Maximum | 35216 | 33223 | 30607 | 21657 | 15750 | 12003 |
| | | 548310 | Therapeutische Monitoring 1/Bloed : Doseren van CA 15 3 met niet isotopenmethode (Maximum 1) (Cumulregel 201, 315) (Diagnoseregel 46) Klass | 82963 | 105286 | 118008 | 141594 | 163434 | 176097 |
| | CA 19-10 | 548354 | Therapeutische Monitoring 1/Bloed : Doseren van carbohydrate antigen 19-9 (CA 19-9) (Maximum 1)(Cumulregel 201)(Diagnoseregel 46) Klasse 20 | 18478 | 22609 | 26091 | 31333 | 36710 | 41700 |
| | CA 19-9 | 436214 | Therapeutische Monitoring 1/Bloed : Doseren van carbohydrate ant | 11356 | 11132 | 8535 | 5589 | 4766 | 3360 |

# FIGURES OF THE IMA SAMPLE

**Figure 2.1sub1 Number of tests per subcluster for anemia tests in function of year (Y-axis scales differ per panel).**

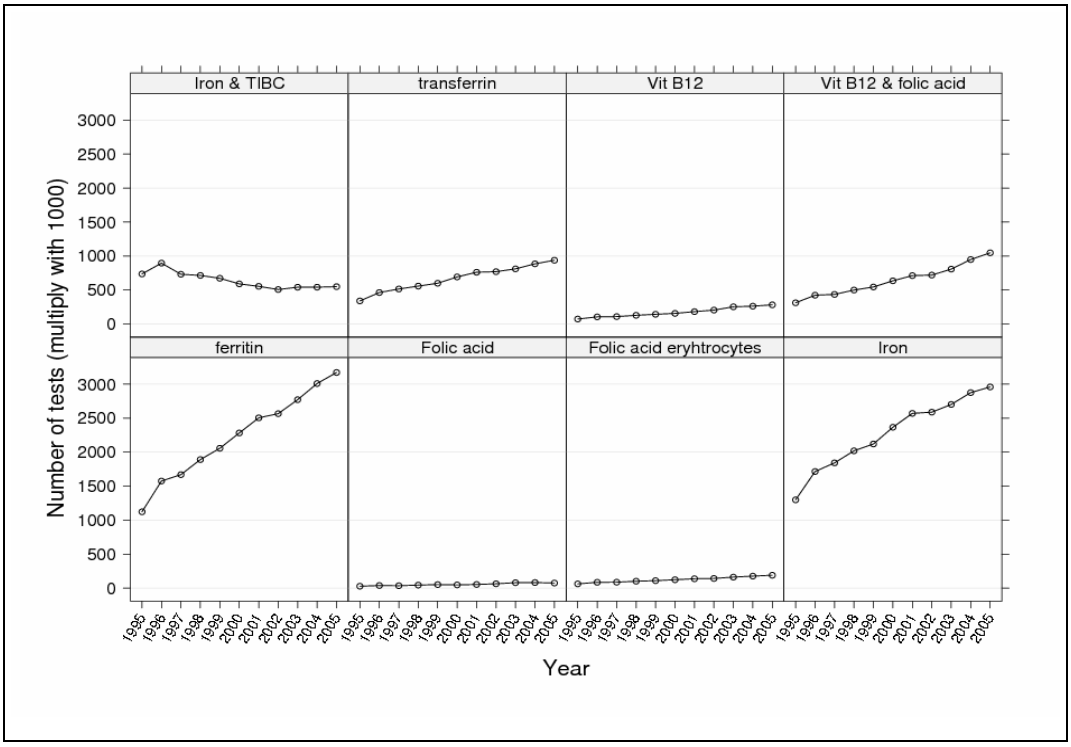



**Figure 2.1sub2 Number of tests per subcluster for diabetes tests in function of year.**

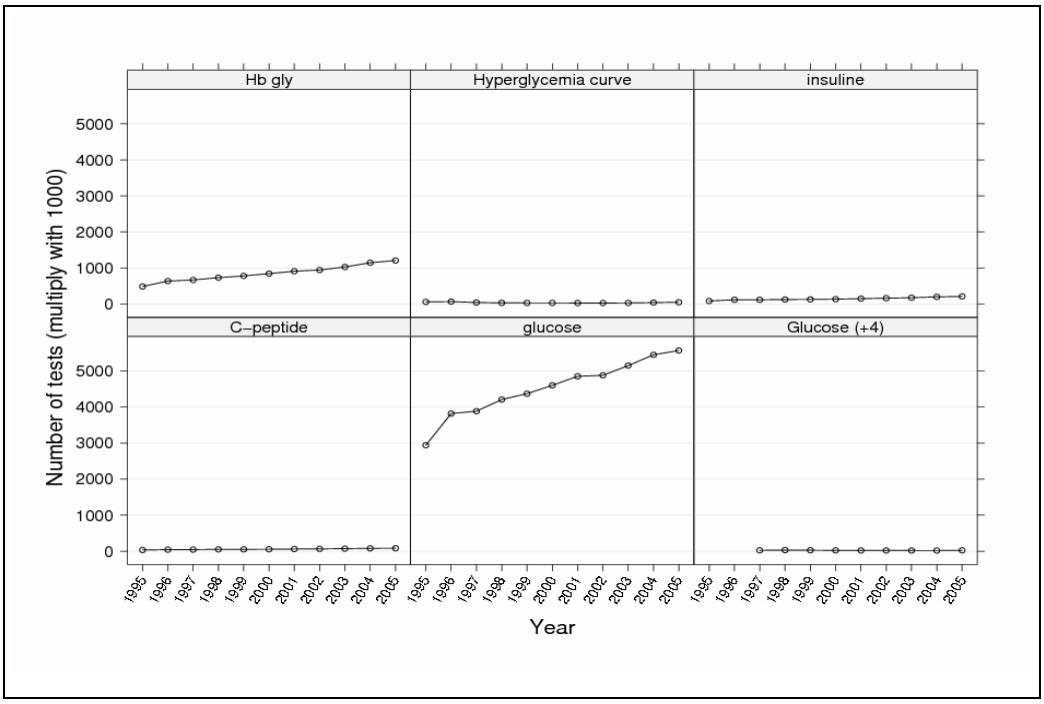


**Figure 2.1sub3 Number of tests per subcluster for liver tests in function of year.**

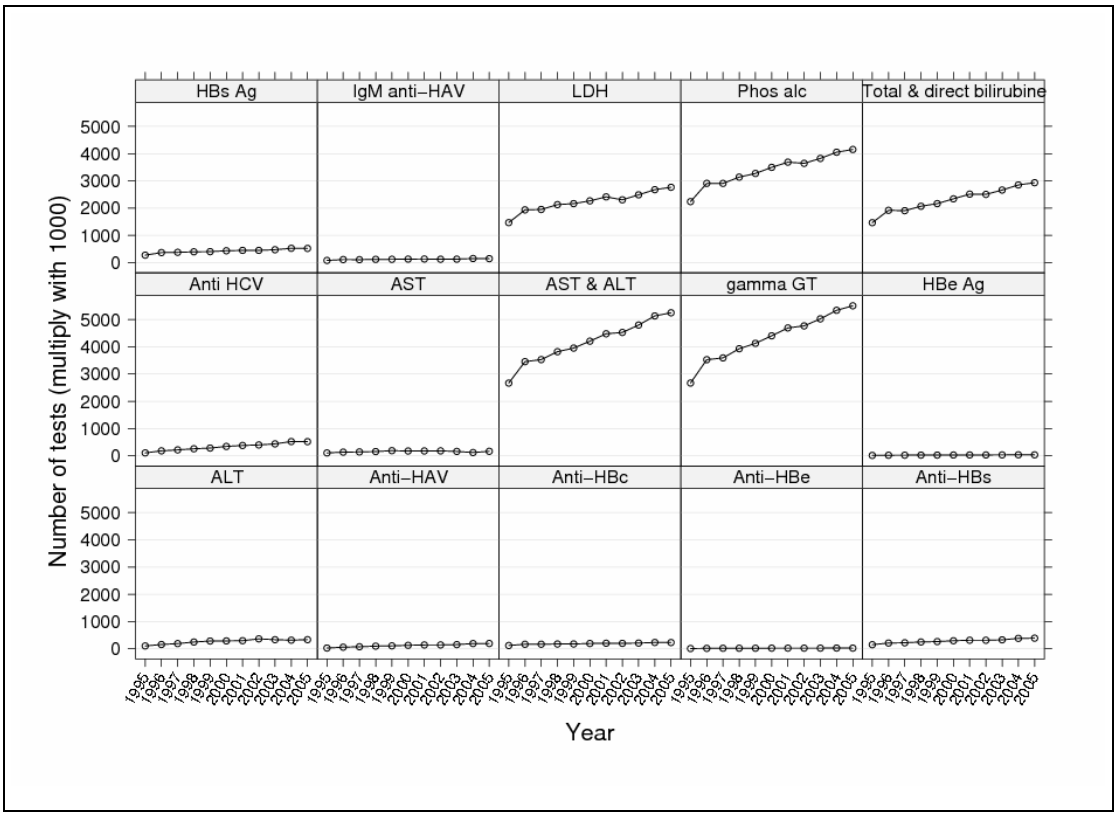



**Figure 2.1sub4 Number of tests per subcluster for thyroid tests in function of year.**

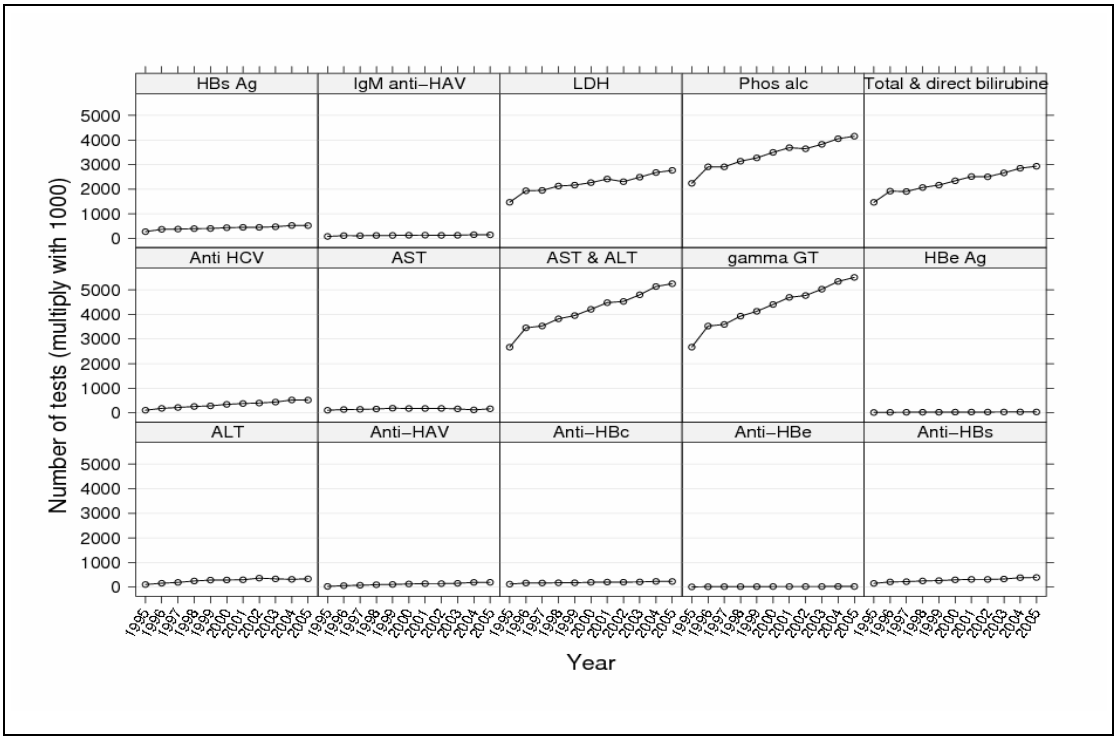


**Figure 2.2sub1 Number of laboratory tests in the IMA sample per year in function of specialism and subclusters of tumour markers**

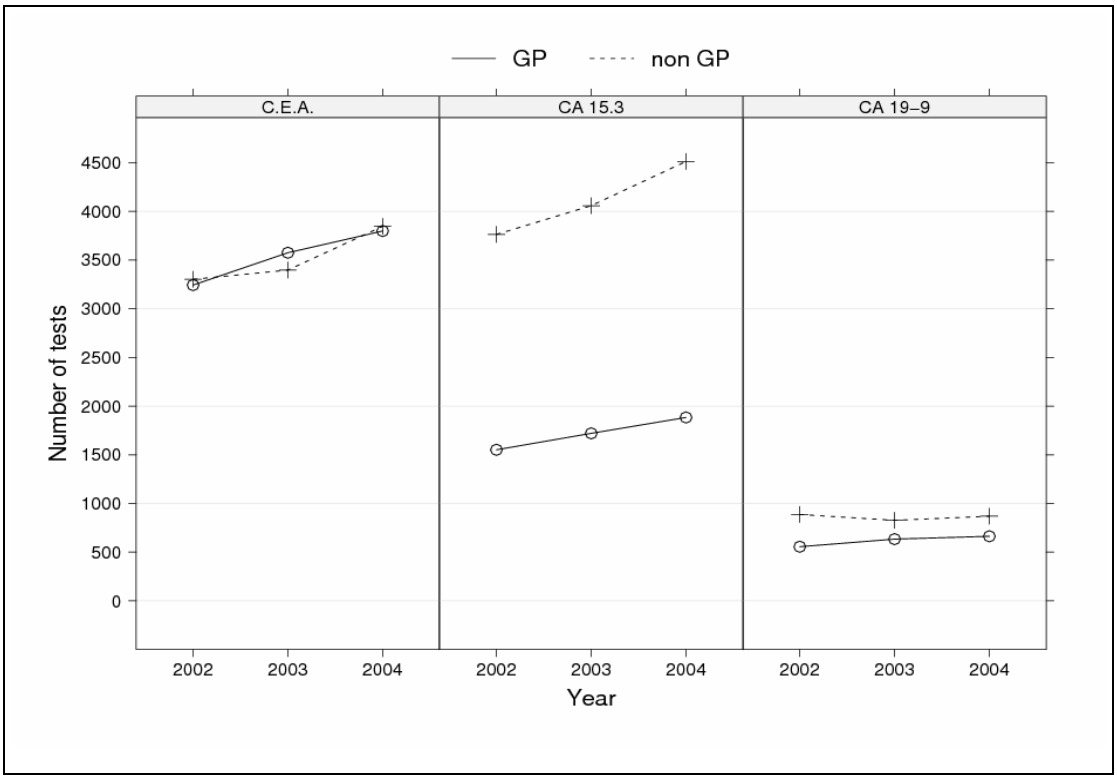



**Figure 2.2sub2 Number of laboratory tests in the IMA sample per year in function of specialism and subclusters of hormonology**

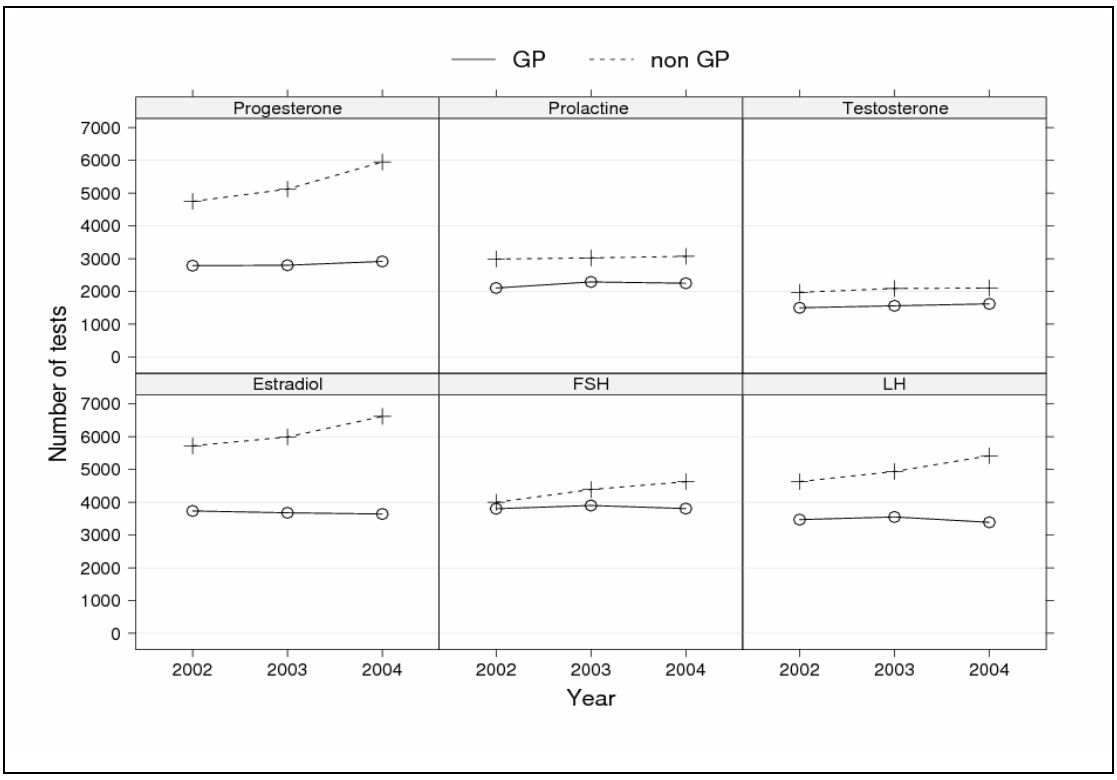


**Figure 2.2sub3 Number of laboratory tests in the IMA sample per year in function of specialism and subclusters of coagulation**

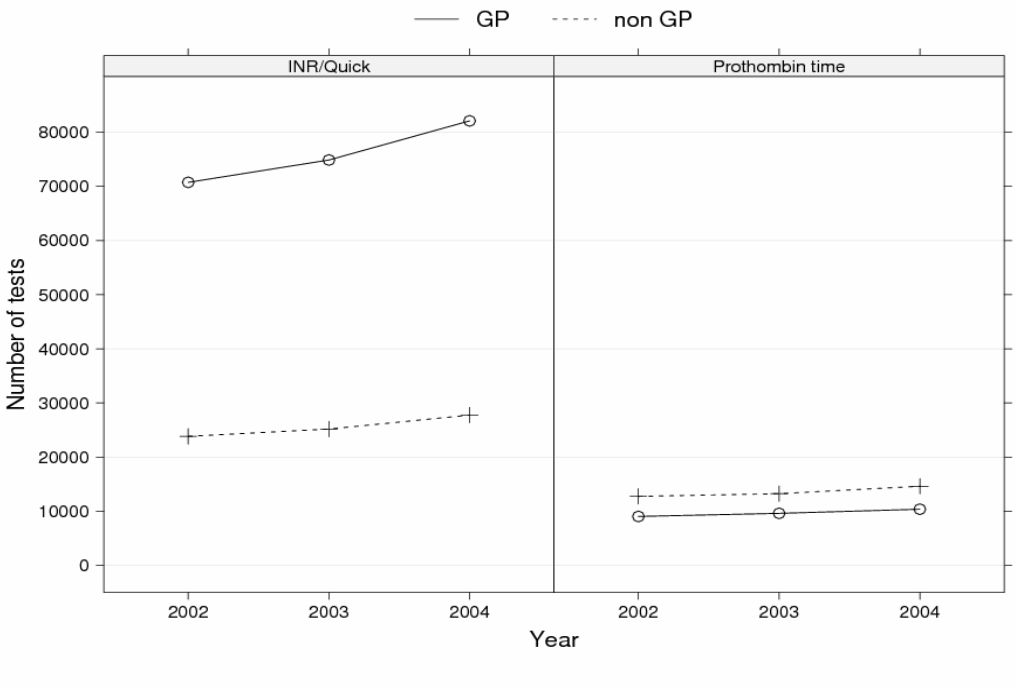



**Figure 2.4sub1 Distribution of number of months between the order of the same laboratory test per patient in the period 2002 – 2004 ordered by GP's in function of laboratory test subcluster for the hormonlogy tests and chronic medication use (whiskers represent minimum and maximum values).**

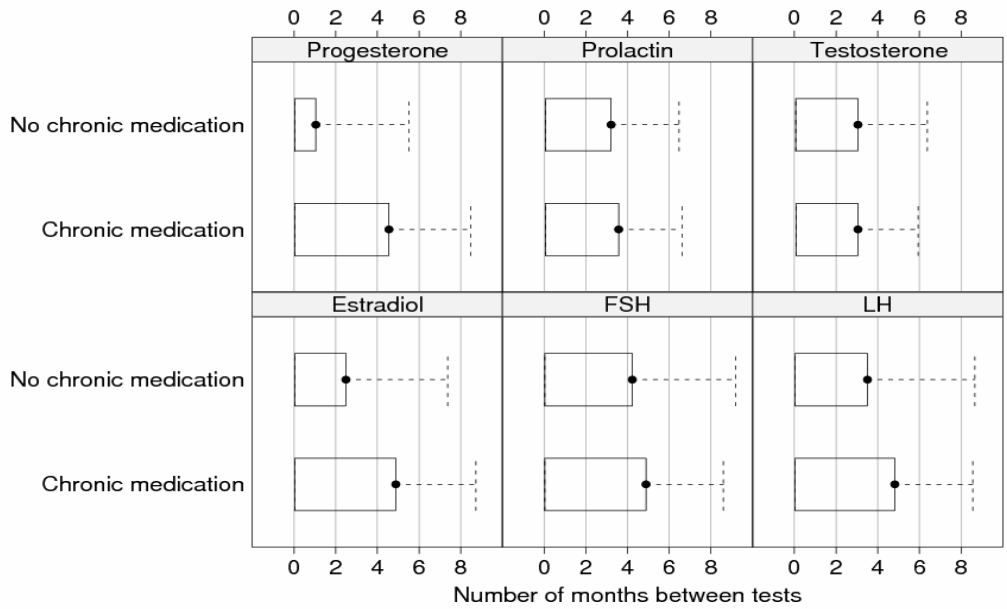
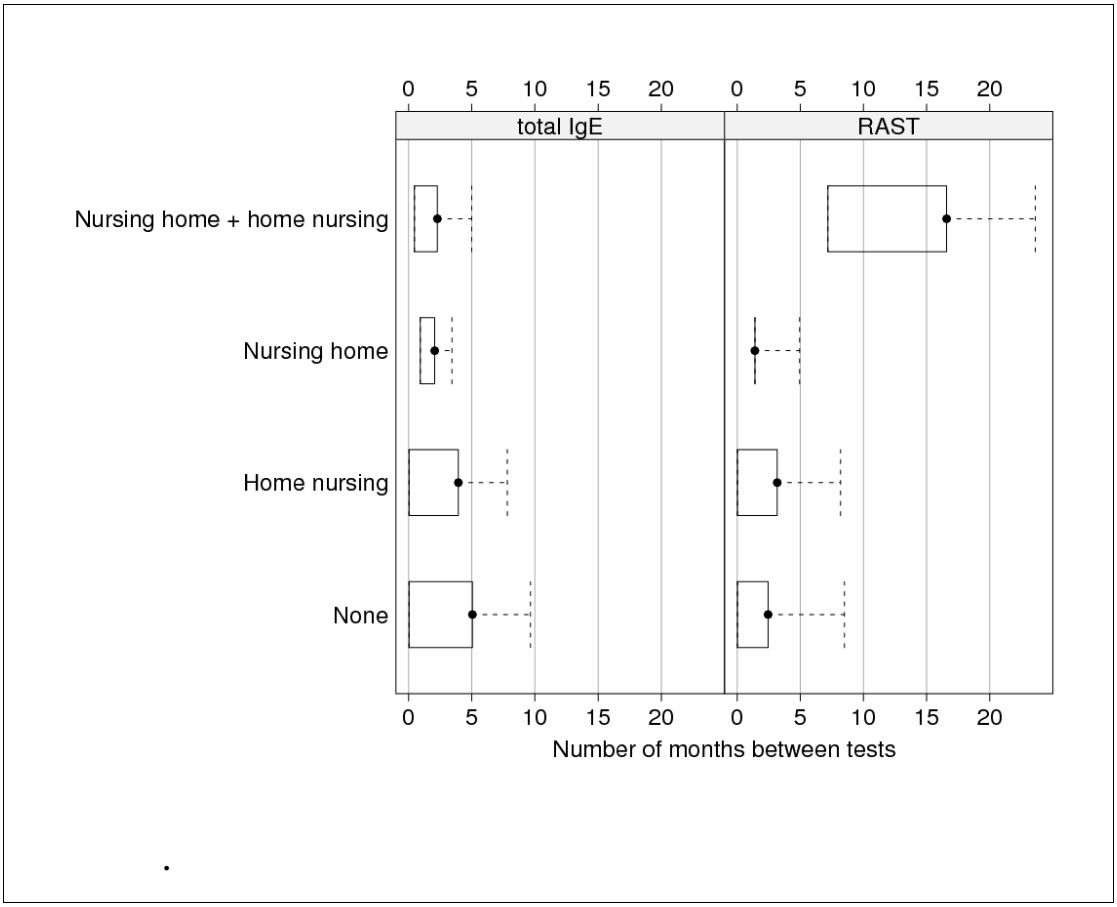


**Figure 2.6sub1 Distribution of number of months between the order of the same laboratory test per patient in the period 2002 – 2004 ordered by GP's in function of subclusters for the allergy tests and care status (whiskers represent minimum and maximum values)**



# CHAPTER 3: APPROPRIATE USE OF LABORATORY TESTS IN GENERAL PRACTICE

**Table 3.1 evidence tables of the included articles**

| **Study ID** | **Carraro**<br>**2003** | **Larsson**<br>**1999** | **Malcolm**<br>**2000** |
|---|---|---|---|
| **Setting** | Outpatient clinic of an academic medical center | General practices | General practice |
| **Definition of (in)appropriate use** | Based on guideline previously published;<br>Antithrombin activity: pregnant women suspected of HELLP syndrome<br>Thrombophilia screening: thrombotic events, late pregnancy with risk factors, thrombosis in cancer, hypertension, sterility, anemia, before oral contraceptives and VTE in family history | Recommendations on appropriate use, by Prof Tryding, based on references to the literature<br>Ratios to decrease or increase listed in article | 15 academic general practitioners served as benchmark of good quality laboratory use |
| **Process of applying criteria** | Clinical information from prescription forms, patient interviews or telephone calls with general practitioners | Ordering habits of doctors were monitored | Clinical vignettes |
| **Laboratory tests assessed (n)** | Antithrombin activity<br>Thrombophilia screening:<br>Protein C<br>Protein S<br>Activated protein C resistance<br>Homocysteinemia<br>Genetic polymorphism of factor V Leiden<br>Mutant prothrombin allele 20210A<br>N=not stated | Extensive list of ratios that were monitored | All possible tests requested by participating physicians |
| **Physicians (n)** | Not stated | 63 doctors at 19 practices | 40 |
| **Patients (n)** | 247+168 | Not stated | Not applicable |
| **Results** | At least 34% inappropriate<br>At least 54% inappropriate | Significant changes in all ratios except 5 | Wide variability in expenditure, mean difference between groups fairly small |

| Study ID | Winkens 1996 | Van Wijk 2001 | Schectman 1992 |
|---|---|---|---|
| Setting | General practice | General practice | Adult practice of primary care service |
| Definition of (in)appropriate use | Based on accepted regional guidelines and standards of the Dutch College of General Practitioners (found in earlier publication, Winkens 1995, Lancet) | Based on guidelines developed by the Dutch Royal College of General Practitioners | TSH as an initial screen, |
| Process of applying criteria | Number of tests for each doctor | Average number of tests per order form per practice<br>Most frequently ordered that accounted for 80% of total number of tests | Pre- and postintervention ordering rates of each thyroid function test/total number of patients for whom any TFT's were ordered |
| Laboratory tests assessed (n) | 44 common tests<br>tests advised against<br>with recommended alternative (urea, thyroxine, free thyroxine, and triiodothyronine concentrations; Rose-Waaler and latex fixation tests)<br>without a recommended alternative (haemoglobin concentration, packed cell volume, differential count, erythrocyte sedimentation rate, leucocyte count, erythrocyte count, lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase) | ALT, AST, total bilirubin, cholesterol, creatinine, ESR, free thyroxine, GGT, glucose, glycosylated hemoglobin, hemoglobin, MCV, Paul-Bunnell, potassium, TSH | Thyroid function tests |
| Physicians (n) | 85 | 62 | 41 clinicians (21 internists, 1 family practitioner, 5 internal medicine residents and 14 physician assistants and nurse practitioners) |
| Patients (n) | Not stated | 77 336 | Mean of 29 patients per clinician |
| Results | Number of tests decreased by 29% between 1984-1993<br>Tests with a recommended alternative decreased by 85%<br>Tests without an alternative by 46% | 20% fewer tests using guideline based software | TSH increased by 42%, T4 decreased by 36%, T3 by 12% and T3RU by 21%. |

| Study ID | Bailey 2005 | Zaat 1992 | Van Gend 1996 |
|---|---|---|---|
| Setting | General practice | General practice | General practice |
| Definition of (in)appropriate use | Tests more appropriate for hospital use were removed from the request form | Literature on sensitivity and specificity in low prevalence populations showed only 15 tests to be useful | Tests that contribute most to making diagnoses, based on the NHG guidelines: Hb, aPTT, PT, thrombocytes, □-GT, ALT, bilirubin, creatinine, sedimentation rate, uric acid, mononucleosis test, cholesterol, TSH, fasting glucose, postprandial glucose, K, phadatiop |
| Process of applying criteria | Incidence ratios comparing the request rate for each test before and after the new form | Total number of tests ordered per GP per 1000 patients, calculated separately for the 15 tests and the remaining tests | Before-after analysis for the total number of tests requested |
| Laboratory tests assessed (n) | CRP, rheumatoid factor, LDH, serum calcium | Hb, fasting glucose, postprandial glucose, HbA1c, □-GT, ALT, AST, total bilirubin, K, mononucleosis test, creatinine, cholesterol, sensitive TSH, T4<br>Remaining tests: usual form of 178 tests | Hb, AST, leukocytes, Hct, AF, erythrocytes, ureum, T4, LDH, sedimentation rate |
| Physicians (n) | Not stated | 75 | Approximately 70 GPs |
| Patients (n) | NHS Trust serving approximately 500 000 in the area | Not stated | Not stated |
| Results | Incidence ratio<br>Calcium 0.38<br>LDH 0.21<br>RF 0.73<br>CRP 0.70 | Average number of tests decreased by 18% with restricted form in intervention group, mainly for tests no longer on the form | Average number of tests decreased by 23%, ranging from 79% for erythrocytes to 7% for sedimentation |

# CHAPTER 5: PROSPECTIVE STUDY

**Table 5.2: frequencies of the 60 tests**

| TEST | % |
|---|---|
| Hb | 63.9 |
| WBC | 63.3 |
| RBC+HCT | 63.2 |
| WBC differentiation | 58.7 |
| AST+ALT | 57.1 |
| Creatinine | 56.9 |
| Glucose | 55.0 |
| Thrombocytes | 52.8 |
| gammaGT | 50.8 |
| Total CHOL | 47.9 |
| ESR | 46.0 |
| CRP | 44.4 |
| HDL chol | 43.3 |
| Triglycerides | 43.2 |
| TSH | 41.9 |
| Uric acid | 34.2 |
| K | 29.2 |
| Ferritin | 28.7 |
| Na | 28.6 |
| Alkaline phosphatase | 28.2 |
| PT (INR/Quick) | 27.3 |
| Urea | 25.3 |
| Fe | 23.2 |
| Total protein | 17.5 |
| Cl | 16.7 |
| Bil tot+fract | 16.1 |
| Vit B12+FZ | 15.0 |
| FT4 | 14.9 |
| Amylase | 13.7 |
| HbA1c | 13.5 |
| LDH | 13.2 |
| Ca | 13.0 |
| Lipase | 10.2 |
| Protein electrophoresis | 8.7 |
| Phosphate | 8.3 |
| CK | 8.2 |
| Transferrin | 7.9 |
| Bicarbonate | 7.0 |
| Mg | 6.9 |
| FT3 | 5.4 |
| Reticulocytes | 5.3 |
| HIV-Ab | 4.1 |
| Fe+TIBC | 3.8 |

| | |
|---|---|
| ABO+Rh | 3.6 |
| Total IgE | 3.0 |
| HBsAg | 2.9 |
| RF | 2.8 |
| HCV-Ab | 2.4 |
| HBsAb | 2.3 |
| Total bilirubine | 2.3 |
| RAST | 2.2 |
| Fibrinogen | 2.0 |
| APTT | 2.0 |
| CMV-IgG | 1.8 |
| Toxopl IgG | 1.7 |
| Toxopl IgM | 1.6 |
| CMV-IgM | 1.6 |
| LH | 0.9 |
| Progesterone | 0.8 |
| Estradiol | 0.8 |

**Table 5.5: diseases most frequently followed-up (N=1915)**

| | N |
|---|---|
| Lipid metabolism | 289 (15.1) |
| Atrial fibrillation/flutter | 232 (12.1) |
| Hypertension, uncomplicated | 182 (9.5) |
| Diabetes | 172 (9.0) |
| Hypothyroidism/myxoedema | 63 (3.3) |
| Pulmonary embolism | 47 (2.5) |
| Heart valve disease NOS | 43 (2.3) |
| Chronic alcohol abuse | 37 (1.9) |
| Anaemia | 36 (1.9) |
| Ischemic heart disease without angina | 33 (1.7) |
| Stroke, cerebrovascular accident | 32 (1.7) |
| Chronic renal failure | 28 (1.5) |
| Abnormal glucose tolerance | 27 (1.4) |
| Heart failure | 25 (1.3) |
| Phlebitis, thrombophlebitis | 25 (1.3) |
| Overweight | 25 (1.3) |
| Worms/other parasites | 22 (1.2) |
| Ischemic heart disease with.angina | 22 (1.2) |
| Rheumatoid /seropositive arthritis | 20 (1.0) |

**Table 5.6: complaints/working hypotheses considered**

| | N | % |
|---|---|---|
| Weakness, general fatigue | 118 | 20.5 |
| Weight loss | 24 | 4.2 |
| Joint symptoms/complaints not otherwise specified | 22 | 3.8 |
| Fever | 18 | 3.1 |
| Respiratory infection other | 18 | 3.1 |
| Feeling ill | 16 | 2.8 |
| Abdominal pain/localised other | 15 | 2.6 |
| Cough | 13 | 2.3 |
| Allergy/allergic reactions not otherwise specified | 12 | 2.1 |
| Muscle pain | 12 | 2.1 |
| Abdominal pain/cramps general | 11 | 1.9 |
| Vertigo, dizziness | 11 | 1.9 |
| Pneumonia | 10 | 1.7 |
| Chest pain not otherwise specified | 9 | 1.6 |
| Menopausal symptoms/complaints | 8 | 1.4 |
| Pain, general multiple sites | 7 | 1.2 |
| Chronic alcohol abuse | 7 | 1.2 |
| Pruritus | 7 | 1.2 |
| Nausea | 6 | 1.0 |
| Palpitations/awareness of heart | 6 | 1.0 |
| Feeling depressed | 6 | 1.0 |
| Weight gain | 6 | 1.0 |

**Table 5.8: additional reason for testing when main reason is general check-up/prevention**

| | Additional reason "follow-up" | Additional reason "diagnostic work-up" |
|---|---|---|
| | Clinical reasons/diseases | Complaints/working hypotheses |
| | (n = 166 in 98 orders) | (n=22 in 19 orders) |
| | N (%) | N (%) |
| Lipid profile, follow-up | 60 (36.1) | - |
| Hypertension | 43 (25.9) | - |
| Endocrine/metabolic and nutritional (T) | 19 (11.5) | - |
| Weakness/general fatigue (A) | - | 3 (13.6) |
| Psychological (P) | 10 (6.0) | 3 (13.6) |
| Respiratory (R) | - | 3 (13.6) |
| Digestive (D) | 9 (5.4) | - |
| Cardiovascular* (K) | 8 (4.8) | - |
| Musculoskeletal (L) | 6 (3.6) | 8 (36.4) |
| Others | 11 (6.6) | 5 (22.7) |

**Table 5.10: test recommended for general check-up, hypertension and cardiovascular risk calculation (follow-up lipid profile)**

| | | Check-up | Hypertension | Cardiovascular risk calculation |
|---|---|---|---|---|
| | % of orders in which the test is requested | Recommended | Nr of guidelines which recommend the test (n=4) | Nr of guidelines which recommend the test (n=4) |
| WBC | 98.1 | | | |
| Hb | 97.4 | 1 | 2 | |
| RBC+HCT | 96.1 | | 2 | |
| Total chol | 96.1 | | 4 | 4 |
| Creatinine | 95.5 | 1 | 4 | |
| Glucose | 95.5 | 1 | 4 | 4 |
| AST+ALT | 95.5 | 1 | | |
| WBC differentiation | 93.3 | | | |
| Gamma GT | 92.3 | | 1 | |
| Triglycerides | 91 | | 1 | 3 |
| HDL chol | 90.3 | | 3 | 4 |
| Platelets | 87.7 | | | |
| TSH | 78.7 | 1 | 1 | |
| Uric acid | 67.1 | | 2 | |
| ESR | 67.1 | 1 | | |
| CRP | 64.5 | | | |
| Ferritin | 50.3 | | | |
| Alk phosph | 49 | | | |
| K | 47.1 | | 4 | |
| Na | 46.5 | | | |
| Urea | 44.5 | | | |
| Fe | 41.9 | | | |
| Total protein | 39.4 | | | |
| Cl | 34.2 | | | |
| Ca | 29 | | 1 | |

**Table 5.12: main reason for testing in cases where clinical motivation is diabetes non insulin dependent or glucose intolerance**

| N=257 | N | % |
|---|---|---|
| Follow-up | 180 | 70.0 |
| Diagnostic work-up | 33 | 12.8 |
| General check-up/prevention | 18 | 7 |
| In preparation of consult with specialist | 8 | 3.1 |
| By request of specialist | 7 | 2.7 |
| Worried patient/parent | 5 | 2.0 |
| Cardiovascular check-up | 3 | 1.2 |
| Explicit request of the patient | 2 | 0.78 |
| Pre operative examination | 1 | 0.39 |

**Table 5.13: additional reasons for testing besides diabetes**

| | Additional clinical reasons follow-up (N=261) | Additional clinical reasons diagnostic work-up (N=38) |
|---|---|---|
| Cardiovascular | 161 (61.7) | 1 (2.6) |
| Endocrine/metabolic/nutritional (not T90) | 22 (8.4) | 8 (21.1) |
| Blood, blood forming organs and immune mechanism | 13 (5.0) | 4,98 |
| Urological | 12 (4.6) | 2 (5.3) |
| Muscoloskeletal | 12 (4.6) | 7 (18.4) |
| Psychological | 10 (3.8) | 3,83 |
| Male genital | 8 (3.1) | 3,07 |
| Respiratory | 8 (3.1) | 5 (13.2) |
| Digestive | 7 (2.7) | 4 (10.5) |
| Skin | 3 (1.2) | 1 (2.6) |
| Female genital | 3 (1.2) | 1 (2.6) |
| Neurological | 1 (0.38) | 2 (5.3) |
| General and unspecified | 1 (0.38) | 7 (18.4) |

**Table 5.15: Tests recommended for diabetes and cardiovascular indications**

| | % of orders in which the test is requested | diabetes* | hypertension | Lipid profile/ cardiovasc risk calculation | Atrial fibrillation/flutter |
|---|---|---|---|---|---|
| Glucose | 92.2 | 5**** | 4 | 4 | 1 |
| HbA1c | 82.0 | 3 | | | |
| Creatinine | 66.8 | 4 | 4 | | 2 |
| Hb | 62.4 | | 2 | | 1 |
| RBC+Hct | 62.0 | | 2 | | 1 |
| WBC | 62.0 | | | | |
| AST+ALT | 56.6 | | | (1)** | (1)*** |
| WBC Differentiation | 55.1 | | | | |
| Total chol | 54.6 | 4 | 4 | 4 | |
| Platelets | 52.7 | | | | |
| Triglycerides | 51.2 | 4 | 1 | 3 | |
| HDL chol | 49.3 | 4 | 3 | 4 | |
| Gamma GT | 47.3 | | 1 | | |
| ESR | 44.9 | | | | |
| CRP | 42.4 | | | | |
| Uric acid | 41.5 | | 2 | | |
| K | 40.5 | 1 | 4 | | 1 |
| Na | 40.0 | 1 | | | |
| TSH | 37.1 | 1 | 1 | | |
| Urea | 28.8 | | | | |

| | | | | |
|---|---|---|---|---|
| Alk phosph | 26.8 | | | |
| Ferritin | 25.4 | | | |
| Cl | 22.4 | | | |
| Fe | 20.0 | | | |
| Ca | 16.6 | I | | |
| PT (INR/Quick) | 16.1 | | | I |
| Total protein | 16.1 | | | |
| Bil tot+fract | 13.7 | | | |
| Vit B12+FZ | 13.7 | | | |
| LDH | 12.7 | | | |
| FT4 | 12.2 | | | |
| CK | 11.7 | | (1)** | |
| APTT | 0.49 | | | (1) |

*All tests: diagnosis and annual follow-up. Monitoring glycemic control : Glc, HbA1c

** Recommended only in case of treatment with statins

*** Recommended only when coagulation therapy is planned, not as follow-up test

**** number of guidelines recommending the test

**Table 5.19: reasons for testing in cases when clinical motivation is hypertension**

| Reason for testing (main or additonal) | N | % |
|---|---|---|
| follow-up | 182 | 51.4 |
| check-up | 70 | 19.8 |
| diagnostic work-up | 51 | 14.4 |
| in preparation of consult with specialist | 12 | 3.4 |
| explicit request of the patient | 13 | 3.7 |
| cardiovascular check-up | 7 | 2.0 |
| pre-operative examination | 7 | 2.0 |
| by order of specialist | 6 | 1.7 |
| worried patient/parent | 5 | 1.4 |
| for insurance/visa/work/school | 1 | 0.28 |
| | 354 | |

**Table 5.28: Main reasons for performing laboratory investigations with order for urea (n=399).**

| | N (%) |
|---|---|
| Follow-up of chronic disease or treatment | 152 (40.6) |
| Diagnostic work-up | 105 (26.3) |
| Check-up / prevention | 69 (17.3) |
| Explicit request of patient | 23 (5.8) |
| Pre-operative investigation | 15 (3.8) |
| Other | 11 (2.6) |
| Cardiovascular check-up | 9 (2.3) |
| Worried patient/parent | 5 (1.3) |

**Table 5.29: clinical reasons for requesting lab tests containing urea (N = 660)**

| | | |
|---|---|---|
| **Complaints/working hypotheses for which a laboratory test order with urea was ordered, ICPC classified.** | | **N=184** |
| General and unspecified | Total | 57 (31) |
| | Weakness/general fatigue | 54 |
| | Other | 3 |
| Muscoloskeletal | | 29 (16) |
| Endocrine/metabolic and nutritional | | 21 (11) |
| Respiratory | | 20 (11) |
| Digestive | | 12 (7) |
| Neurological | | 10 (5) |
| Psychological | | 8 (4) |
| Blood, bloodforming organs and immune mechanism | | 6 (3) |
| Cardiovascular | | 5 (3) |
| Skin | | 5 (3) |
| Female genital | | 4 (2) |
| Urological | | 3 (2) |
| Male genital | | 3 (2) |
| Pregnancy, childbearing, family planning | | 1 (1) |
| **Diseases followed for which urea was ordered. N=433** | | |
| Cardiovascular | Total | 185 (43) |
| | Follow up lipid metabolism | 106 |
| | Other | 79 |
| Endocrine/metabolic and nutritional | Total | 108 (25) |
| | Diabetes non insulin dependent /glucose intolerance | 58 |
| | Other | 50 |
| Psychological | | 28 (6) |
| Muscoloskeletal | | 20 (5) |
| Digestive | | 18 (4) |
| Chronic renal failure | | 18 (4) |
| Female genital | | 17 (4) |
| Respiratory | | 12 (3) |
| Blood, bloodforming organs and immune mechanism | | 10 (2) |
| Male genital | | 10 (2) |
| General and unspecified | | 3 (1) |
| Skin | | 3 (1) |
| Eye | | 1 (0) |
| **Therapeutic monitoring for which urea was ordered, N = 43** | | |
| Anticoagulants | | 10 (23) |
| Other | | 33 (77) |

**Table 5.30: clinical reasons for performing laboratory investigations with orders for total protein (n=493)**

| **Complaints/working hypotheses for which a laboratory test order with total protein was ordered, n=163** | | **N (%)** |
|---|---|---|
| General/unspecified | Total | 51 (31.3) |
| | Weakness/general fatigue | 30 |
| | Other | 21 |
| Musculoskeletal | | 29 (17.8) |
| Respiratory | | 23 (14.1) |
| Endocrine/metabolic and nutritional | | 16 (9.8) |
| Blood, blood forming organs and immune mechanism | | 7 (4.3) |
| Digestive | | 7 (4.3) |
| Psychological | | 7 (4.3) |
| Skin | | 6 (3.7) |
| Neurological | | 5 (3.1) |
| Pregnancy, childbearing, family planning | | 4 (2.5) |
| Cardiovascular | | 3 (1.8) |
| Female genital | | 3 (1.8) |
| Urological | | 1 (0.61) |
| Male genital | | 1 (0.61) |
| **Conditions followed with laboratory orders in which total protein was ordered, n=327** | | **N (%)** |
| Cardiovascular | Hypertension | 59 |
| | Lipid metabolism | 65 |
| | Other | 37 |
| | Total | 161 (49.2) |
| Endocrine/metabolic and nutritional | Total | 66 (20.2) |
| | Diabetes | 31 |
| | Other | 35 |
| Musculoskeletal | | 18 (5.5) |
| Digestive | | 17 (5.2) |
| Blood, bloodforming organs and immune mechanism | | 15 (4.6) |
| Psychological | | 13 (4.0) |
| Respiratory | | 12 (3.7) |
| Urological | | 10 (3.1) |
| Neurological | | 4 (1.2) |
| Skin | | 4 (1.2) |
| Male genital | | 4 (1.2) |
| General/unspecified | | 3 (0.92) |
| **Follow-up of treatment medication, n=3** | | **N (%)** |
| | | 3 (0.92) |

**Table 5.31: clinical reasons for performing laboratory investigations with order for amylase (n=423)**

| **Complaints/working hypotheses for which a laboratory test order with amylase was** |
|---|

| **ordered, ICPC classified (n=131)** | | |
|---|---|---|
| | | N (%) |
| General/unspecified | Total | 42 (32.1) |
| | Weakness/general fatigue | 28 |
| | Other | 14 |
| Digestive | | 22 (16.8) |
| Musculoskeletal | | 16 (12.2) |
| Endocrine/metabolic and nutritional | | 14 (10.7) |
| Respiratory | | 13 (9.9) |
| Neurological | | 6 (4.6) |
| Skin | | 5 (3.8) |
| Cardiovascular | | 5 (3.8) |
| Psychological | | 3 (2.3) |
| Blood, bloodforming organs and immune mechanism | | 2 (1.5) |
| Pregnancy, childbearing, family planning | | 2 (1.5) |
| Female genital | | 2 (1.5) |
| Urological | | 1 (0.76) |
| Male genital | | 1 (0.76) |
| **Diseases followed with laboratory orders in which amylase was ordered. N=272** | | |
| | | N (%) |
| Cardiovascular | Total | 137 (50.4) |
| | Hypertension | 31 |
| | Lipid metabolism | 60 |
| | Other | 46 |
| Endocrine/metabolic and nutritional | Total | 46 (16.9) |
| | Diabetes | 17 |
| | Other | 29 |
| Digestive | | 26 (9.6) |
| Psychological | | 15 (5.6) |
| Musculoskeletal | | 12 (4.4) |
| Blood, bloodforming organs and immune mechanism | | 12 (4.4) |
| Male genital | | 5 (1.8) |
| General/unspedified | | 5 (1.8) |
| Respiratory | | 4 (1.5) |
| Urological | | 4 (1.5) |
| Skin | | 3 (1.1) |
| Female genital | | 2 (0.74) |
| Neurological | | 1 (0.37) |
| **Follow-up of treatment medication (n=20)** | | |
| Anticoagulants | | 5 (25.0) |
| Other | | 15 (75.0) |

**Table 5.32: clinical reasons for performing laboratory investigations with order for platelet count (n=1569)**

| **Complaints/working hypotheses for which a laboratory test order with platelet count was ordered, ICPC classified (n=426)** | | **N (%)** |
|---|---|---|
| General/unspecified | Total | 162 (38.0) |

| | | |
|---|---|---|
| | Weakness/general fatigue | 96 |
| | Other | 68 |
| Digestive | | 43 (10.1) |
| Musculoskeletal | | 49 (11.5) |
| Endocrine/metabolic and nutritional | | 37 (8.7) |
| Respiratory | | 50 (11.7) |
| Neurological | | 19 (4.5) |
| Skin | | 18 (4.2) |
| Cardiovascular | | 13 (3.1) |
| Psychological | | 6 (1.4) |
| Blood, blood a forming organs and immune mechanism | | 6 (1.4) |
| Pregnancy, childbearing, family planning | | 6 (1.4) |
| Female genital | | 11 (2.6) |
| Urological | | 3 (0.70) |
| Male genital | | 2 (0.47) |
| Eye | | 1 (0.23) |

**Diseases followed with laboratory orders in which platelet count was ordered. N=1038**

| | | N (%) |
|---|---|---|
| Cardiovascular | Total | 460 (44.3) |
| | Hypertension | 135 |
| | Lipid metabolism | 193 |
| | Other | 132 |
| Endocrine/metabolic and nutritional | Total | 214 (20.6) |
| | Diabetes | 105 |
| | Other | 109 |
| Digestive | | 57 (5.5) |
| Psychological | | 56 (5.4) |
| Musculoskeletal | | 48 (4.6) |
| Blood, bloodforming organs and immune mechanism | | 63 (6.1) |
| Male genital | | 5 (1.8) |
| General/unspedified | | 17 (1.6) |
| Respiratory | | 29 (2.8) |
| Urological | | 30 (2.9) |
| Skin | | 11 (1.1) |
| Female genital | | 21 (2.0) |
| Neurological | | 6 (0.58) |
| Male genital | | 24 (2.31) |
| Eye | | 1 (0.1) |
| Ear | | 1 (0.1) |

**Follow-up of treatment medication (n=105, 119 medications)**

| | |
|---|---|
| Anticoagulants | 43 (36.1) |
| Chemotherapy | 18 (15.1) |
| Other | 63 (52.9) |

**Table 5.33: clinical reasons for performing laboratory investigations with order for chlorine (n=577)**

**Complaints/working hypotheses for which a laboratory test order with chloride was ordered, ICPC classified (n=407)**

| | | N (%) |
|---|---|---|
| General/unspecified | Total | 44 (33.9) |

| | | |
|---|---|---|
| | Weakness/fatigue, general | 26 |
| | Other | 18 |
| Musculoskeletal | | 19 (14.6) |
| Endocrine/metabolic/nutritional | | 18 (13.9) |
| Respiratory | | 11 (8.5) |
| Digestive | | 7 (5.4) |
| Neurological | | 5 (3.9) |
| Psychological | | 5 (3.9) |
| Skin | | 5 (3.9) |
| Female genital | | 5 (3.9) |
| Cardiovascular | | 4 (3.1) |
| Urological | | 3 (2.3) |
| Blood/bloodforming organs/immune mechanisms | | 2 (1.5) |
| Pregnancy:child bearing/family planning | | 1 (0.77) |
| Male genital | | 1 (0.77) |

**Diseases followed with laboratory orders in which chloride was ordered. N=130**

| | | N (%) |
|---|---|---|
| Cardiovascular | Total | 198 (48.7) |
| | Hypertension | 68 |
| | Lipid metabolism | 68 |
| | Other | 63 |
| Endocrine/metabolic and nutritional | Total | 85 (20.9) |
| | Diabetes | 42 |
| | Other | 43 |
| Digestive | | 29 (7.1) |
| Respiratory | | 29 (2.8) |
| Male genital | | 24 (2.3) |
| Urological | | 23 (5.7) |
| Psychological | | 20 (4.9) |
| Musculoskeletal | | 18 (4.4) |
| Blood, bloodforming organs and immune mechanism | | 16 (3.9) |
| Male genital | | 5 (1.8) |
| General/unspecified | | 4 (0.98) |
| Female genital | | 3 (0.74) |
| Neurological | | 3 (0.74) |
| Skin | | 1 (0.25) |

**Follow-up of treatment with medication n= 40 (47 medications)**

| | |
|---|---|
| Anticoagulants | 16 (34.0) |
| Other | 31 (65.1) |

# CHAPTER 6: INTERVENTIONS TO INFLUENCE LABORATORY TEST UTILISATION

**Table 6.1: evidence tables of included studies**

| Study | Study type | Quality | Evidence level | Intervention type | Results | Comments |
|---|---|---|---|---|---|---|
| Systematic review : all physicians | | | | | | |
| Solomon 1998[27] | SR | High | 1a | mixed strategy | Interventions based on multiple behavioural factors are more successful<br><br>Nearly every strategy has had both success and failure, providing limited guidance for designing new or more effective strategies. | Methodological flaws hamper drawing strong conclusions. |
| Feedback or guidelines | | | | | | |
| Winkens [16] (Maastricht) | NRCT | valid | 2a | continuous 6-month feedback along 9 years | 54% decrease for 44 common tests along 9 years (mean annual decrease 6%) p< 0.001 | strongest effects are achieved when feedback is repeated , feedback needs to be continuous (general learning effect) |
| Flottorp 2002 [41] (Norway) | cluster RCT | valid | 1b | No feedback, guidelines alone+ computer based decision support and reminders | little impact (5% decrease in use of laboratory for urinary tract) p= 0,046 | Inadequate time, resources and support. Problems with internal communication. Only 33% of practices discuss the guidelines.[30] |
| Baker [29] (UK) | RCT | valid | 1b | guideline sent first for the lead of the team, then feedback for complete practice | feedback alone did not have influence on test ordering | Impossibility to relate tests to individual practitioners (intervention at a practice level). Wide variation between practices. More intensive strategies may be required to change the use of laboratory tests. |
| Wim H. J. M. Verstappen | RCT | valid | 1b | physicians in small groups discussed | number of test in arm A : 12% reduction | Dutch physicians already order fewer tests than in others countries. |

| | | | | | | |
|---|---|---|---|---|---|---|
| [10] (5 regions in the Netherlands | | | | personal feedback related to 3 EB guidelines (3x/6 months) | number of test in arm B : not significant<br>inappropriate tests in arm A : significant reduction<br>inappropriate test in arm B : not significant<br>(arm A : tests for CV topics and abdominal complaints ) | |
| Thomas Ruth [33] (UK) | cluster RCT | valid | 1b | quarterly feedback or educational messages as reminder or both | more than 20% reduction in the total test requested for interventions in combination<br>feedback odds ration : 0.87, 95%CI 0.81-0.94) , (reminders odds ration : 0.89, 95%CI 0.83-0.93), | Neither intervention was consistently better than other |
| Computer<br>Van Wijk 2001 (Delft) | RCT | valid | 1b | comparison from BloodLink-Restricted and BloodLink Guideline : indication-oriented order form versus restricted list | 20% fewer tests with BL Guideline | the introduction of BL was facilitated by the fact that the general practitioners were already using computer-based patient records |
| Test form<br>Zaat 1992 ( Netherlands, different areas) | control trial (NRCT) | valid | 2a | restricted test request form, versus "old" standard form | tests ordered was reduced by 18% (p> 0.001) | the effects are only partly permanent: physicians returned to previous behaviour when reintroducing old form |
| Smithuis 1994 (Deurne) | NRCT | valid | 1b | restricted test request form based on guidelines | significant reduction in 3 tests on 6 | bias? region received intervention with problem oriented form in 1990 |

| | | | | | | |
|---|---|---|---|---|---|---|
| van Gend 1996 (Venlo) | NRCT | valid | 2b | restricted test request form accompanied by 6-month feedback | tests ordered was reduced by 23% | Before-after study |
| Bailey 2005 UK | Before-after study | valid | 2b | restricted test request form | significant reduction in request for serum calcium, LDH and CRP | Rheumatoid factor (out of request) decreased first and then increased . Their removal did not have a deleterious effect on appropriate usage. |
| Fundholding | | | | | | |
| Kerr, 1996 New Zealand | NRCT | valid | 2a | comprehensive strategy : active monthly feedback + educational programmes, test form redesing with prices AND incentives suitable for higher priority services | overall savings of 22,7% (period of 13 months)<br>generally statistically trends downwards in the means and standards deviations | effectiveness of comprehensive strategy |
| Van Walraven 1998, Canada (Ontario) | time serie analysis | valid | 2b or 3 ? | 3 interventions : physician guidelines, laboratory requisition form modification, changes to funding policy (stop funding for total thyroxine) | from 58% (urea) to 80% decrease (iron)<br>p<0,001 (except thyroxine and TSH) | valid with methodological objections, retrospective study (6 years) |

# COST ANALYSIS

Note: this analysis was not included in the validation procedure, and has therefore not been reviewed by the validators

## Introduction and aims:

The various chapters in this report suggest that laboratory test requests could decrease while maintaining or even improving quality in patient care.

The aim of this part of the study was to estimate what would be the impact of a decrease in the number of laboratory test requests on the income and expenditures of medical laboratories. Secondly, one of the ways to use laboratory tests more efficiently is to request only a few tests first, and to request additional tests on the same blood sample when the first result is available, e.g. to request a free T4 if the TSH value is abnormal or to request ferritin if the hemoglobin and MCV are low. We wanted to calculate the extra cost for the laboratory when those additional analyses are requested, and the impact on costs and income for these stepwise strategies.

## Costs and income for the individual tests

### *Methods*

Several medical laboratories serving outpatients were contacted but none of them had a model available on which costs simulations could be run. For this reason the data of a laboratory of a large, university hospital were used.

#### COSTS PER TEST

The costs were calculated for the target analytes discussed previously in this study, except for the blood group and rhesus, which is not performed in the laboratory from which the data were obtained. Because some analyte groups (e.g. total bilirubin versus total bilirubin and fractions) overlapped, the cost was calculated for the individual tests. Fifty-six analytes were included.

The tests were grouped by instrument on which the tests were run and subdivision of the lab. The total number of tests and the total amount of income per request or per hospital day were also calculated.

The invoices, personnel costs, depreciation and other costs incurred in 2006 were inventoried. Each cost was attributed to the test (e.g. reagent for that test), the instrument (e.g. depreciation, maintenance contract, common buffers and spare parts) and the subdivision of the laboratory (e.g. personnel costs). For the depreciation, the rules of the hospital, e.g. a depreciation time of 10 years for infrastructure and non medical equipment (e.g. incubators and refrigerators), 5 years for medical instruments and computers and 3 years for software, were used.

The costs per instrument were distributed over the tests in function of the total income per test (number of tests per year x income received for that test), i.e. more frequent tests and costlier tests received a larger part of the common costs than rarer or cheaper tests.

The same was done for the costs per sublaboratory and the common costs of the laboratory (e.g. the costs for blood drawing, the quality manager, etc.).

#### INCOME PER TEST

The income the laboratory received for an individual test was calculated based on the direct reimbursement for that particular test and a proportion of the forfaitary reimbursement. As already discussed, reimbursement in Belgium constitutes of a direct sum for a particular test and a forfaitary sum for administrative costs and consulting, depending on the sum of all B values of the entire order. The income was thus calculated based on the income per test and (1) the income per sample (for outpatients), or (2) per admission and per hospital day (for inpatients), ventilated over

the different tests in function of their income. This was called the theoretical income, because the real income per request depends on the number of requested tests and their B-value.

*Results:*

We classified 5618 invoices, which covered 3400 different products and services. The costs were ventilated over 5 different laboratory departments (core lab, serology, hormonology, special chemistry and a common category for the other departments), and the general services of the laboratory that serve all departments. Fourteen different instruments were involved in this calculation.

This calculation is shown for the coagulation tests as an example in tables 1 and 2. These tests are performed in the core lab on an instrument that also performs D-dimers, a test that was not included in our list of studied tests. The number of APTT billed is 69,523, and the reimbursement is € 55,922.82. The calculated proportion of the fixed income (per sample, hospital day or admission) is € 126,799.90. The income from APTT is 0.91%, 1.87% and 37.83% of the income of the whole lab, the core lab and the tests run on the instrument respectively. The costs for reagents and supplies for APTT were € 17,853.41. The costs for reagents and supplies for the instrument (e.g. buffers, cuvettes) were € 61,801.79, so the cost attributed to APTT was 37.83% of that amount or € 23,376.61. The same calculation was done for the costs common to the core lab (€ 4,396.53 x 1.87%) and the general costs for the lab (0.91% of € 612,227.74). A similar calculation was performed for the personnel costs (1.87% of € 2,335,231.62) and the ventilation of the personnel costs of the common parts of the lab (e.g. phlebotomists; 0.91% x € 1,793,197.96). And the same calculations were done for the depreciation of the instrument (37.83% x € 14,697.61) and the depreciation costs of the common instruments (e.g. the laboratory information system; 0.91% of € 114,104.96). Finally, the costs for infrastructure are 15.3% of the income. The cost and income per tests are calculated by dividing the total cost and incomes by the number of tests. At the bottom of table 2, the cost percentages for reagents and supplies, personnel, depreciation and infrastructure are given. As the reagent cost per test for D-dimer is much higher, it is relatively more important.

**Table 1: Data used in the income calculation for the coagulation tests.**

| Total cost to be ventilated | APTT | Fibrinogen | PT/INR | Other (D-dimer) |
|---|---|---|---|---|
| **Number of tests performed** | 69,523.00 | 49,164.00 | 78,075.00 | 6,355.00 |
| Income for tests (€) | 55,922.82 | 30,969.49 | 50,712.02 | 10,241.36 |
| Fixed income (€) | 126,799.90 | 70,220.50 | 114,984.89 | 23,221.35 |
| % Total lab | 0.91% | 0.50% | 0.82% | 0.17% |
| % Core lab | 1.87% | 1.04% | 1.70% | 0.34% |
| % Instrument | 37.83% | 20.95% | 34.30% | 6.93% |
| **Income/test (€)** | 2.63 | 2.06 | 2.12 | 5.27 |

**Table 2: Data used in the cost calculation for the coagulation tests.**

| | Total cost to be ventilated | APTT | Fibrinogen | PT/INR | Other (D-dimer) |
|---|---|---|---|---|---|
| **Number of tests performed** | | 69,523.00 | 49,164.00 | 78,075.00 | 6,355.00 |
| % of the income total lab | | 0.91% | 0.50% | 0.82% | 0.17% |
| % of the income core lab | | 1.87% | 1.04% | 1.70% | 0.34% |
| % of the income instrument | | 37.83% | 20.95% | 34.30% | 6.93% |
| **Reagents and supplies** | | | | | |
| Test part (€) | | 17,853.41 | 9,736.21 | 15,151.07 | 49,931.46 |
| Instrument part (€) | 61,801.79 | 23,376.61 | 12,945.73 | 21,198.41 | 4,281.05 |
| Lab part (€) | 4,396.53 | 82.28 | 45.56 | 74.61 | 15.07 |
| General part (€) | 612,227.74 | 5,569.72 | 3,084.45 | 5,050.74 | 1,020.00 |
| **Personnel** | | | | | |
| Core lab part (€) | 2,335,231.62 | 43,701.09 | 24,201.22 | 39,629.09 | 8,003.15 |
| General part (€) | 1,793,197.96 | 16,313.55 | 9,034.28 | 14,793.48 | 2,987.56 |
| **Depreciation** | | | | | |
| Instrument part (€) | 14,697.61 | 5,559.39 | 3,078.73 | 5,041.37 | 1,018.11 |
| General (€) | 114,104.96 | 1,038.07 | 574.87 | 941.34 | 190.10 |
| **Infrastructure (€)** | | 27,956.58 | 15,482.07 | 25,351.63 | 5,119.79 |
| **Total cost** (€) | | 141,450.68 | 78,183.13 | 127,231.74 | 72,566.30 |
| | | | | | |
| **Cost/test (€)** | | 2.03 | 1.59 | 1.63 | 11.42 |
| Reagents & supplies % | | 33.14% | 33.01% | 32.60% | 76.13% |
| Personnel % | | 42.43% | 42.51% | 42.77% | 15.15% |
| Depreciation % | | 4.66% | 4.67% | 4.70% | 1.66% |
| Infrastructure % | | 19.76% | 19.80% | 19.93% | 7.06% |

The total cost structure of the laboratory is given in table 3.

**Table 3: main cost categories for the medical laboratory.**

| Cost | % |
|---|---|
| Personnel | 51.5 |
| Reagents and supplies | 28.4 |
| Costs for infrastructure, electricity, communication and billing | 17.6 |
| Depreciation | 2.5 |

Table 4 gives the total annual number of tests, cost/test and real (RIZIV/IMAMI) income per test and theoretical income/test for the studied analytes.

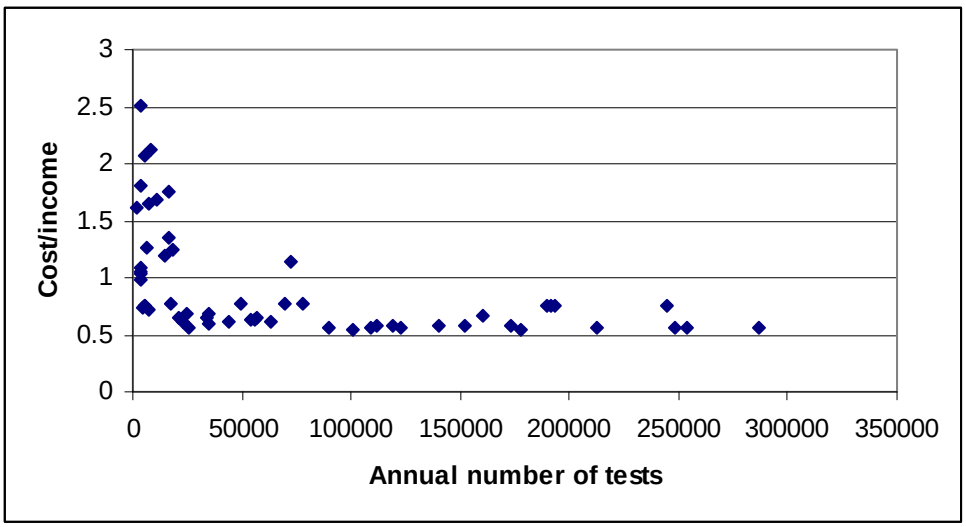
**Table 4: Total annual number of tests, cost/test and real (RIZIV/IMAMI) income per test and theoretical income/test (including the forfaitary payment ventilated over the different tests) calculated on the basis of the data from a hospital-based medical laboratory.**

| Analyte | n | Cost/test (€) | RIZIV/INAMI reimbursement per test (€) | Theoretical income/test (€) |
|---|---|---|---|---|
| Alc. Phosph. | 122747 | 1.19 | 0.58 | 2.11 |
| Amylase | 56627 | 2.15 | 0.91 | 3.28 |
| AST+ALT | 286817 | 1.10 | 1.09 | 1.98 |
| Bilirubin | 22966 | 0.87 | 0.51 | 1.41 |
| Ca | 151638 | 1.21 | 0.58 | 2.10 |
| CK | 54087 | 1.57 | 0.73 | 2.50 |
| Cl | 212488 | 0.88 | 0.44 | 1.57 |
| Creatinine | 177977 | 1.01 | 0.51 | 1.87 |
| CRP | 160516 | 2.25 | 0.91 | 3.36 |
| Fe | 17666 | 2.34 | 0.91 | 3.03 |
| Phosphate | 111749 | 1.04 | 0.51 | 1.78 |
| gammaGT | 119169 | 1.22 | 0.58 | 2.13 |
| Glucose | 139814 | 0.78 | 0.36 | 1.35 |
| K | 253744 | 1.15 | 0.58 | 2.07 |
| LDH | 89571 | 1.15 | 0.58 | 2.05 |
| Lipase | 56111 | 2.06 | 0.91 | 3.28 |
| Mg | 108853 | 1.28 | 0.65 | 2.30 |
| Na | 248634 | 1.02 | 0.51 | 1.82 |
| Total protein | 101092 | 0.71 | 0.36 | 1.30 |
| Triglycerides | 35221 | 1.47 | 0.73 | 2.44 |
| Urea | 173326 | 0.79 | 0.36 | 1.34 |
| Uric acid | 63393 | 0.94 | 0.44 | 1.56 |
| Bicarbonate | 34147 | 1.07 | 0.44 | 1.67 |
| HDLcholesterol | 21200 | 2.35 | 1.09 | 3.63 |
| Total cholesterol | 25518 | 1.08 | 0.58 | 1.93 |
| APTT | 69523 | 2.03 | 0.73 | 2.63 |
| Fibrinogen | 49164 | 1.59 | 0.58 | 2.06 |
| PT/INR | 78075 | 1.63 | 0.58 | 2.12 |
| ESR | 43549 | 0.63 | 0.29 | 1.03 |
| Hemoglobin | 244321 | 0.81 | 0.29 | 1.08 |
| RBC+Hct | 191748 | 0.84 | 0.29 | 1.11 |
| Reticulocytes | 5496 | 1.28 | 0.51 | 1.69 |
| Thrombocytes | 190000 | 0.83 | 0.29 | 1.09 |
| WBC | 193588 | 0.83 | 0.29 | 1.10 |
| WBC differentiation | 71941 | 2.33 | 0.58 | 2.04 |
| HIV Ab | 6697 | 7.76 | 1.82 | 6.12 |
| FT3 | 4560 | 6.44 | 2.55 | 8.67 |
| FT4 | 34568 | 5.77 | 2.55 | 8.54 |
| Progesterone | 5342 | 8.00 | 3.27 | 10.52 |

| Analyte | n | Cost/test (€) | RIZIV/INAMI reimbursement per test (€) | Theoretical income/test (€) |
|---|---|---|---|---|
| TSH | 24843 | 4.17 | 1.82 | 6.11 |
| Estradiol | 7233 | 8.38 | 3.64 | 11.77 |
| CMV IgG | 3963 | 6.10 | 1.82 | 6.19 |
| CMV IgM | 3845 | 7.88 | 2.18 | 7.43 |
| HBs Ab | 5882 | 12.46 | 1.82 | 6.03 |
| HBs Ag | 8096 | 13.07 | 1.82 | 6.15 |
| Hep C Ab | 7616 | 11.27 | 1.82 | 6.44 |
| Toxoplasma IgG | 3840 | 6.27 | 1.82 | 6.05 |
| Toxoplasma IgM | 3982 | 7.85 | 2.18 | 7.24 |
| Protein electrophoresis | 16593 | 8.40 | 1.45 | 4.79 |
| Ferritin | 18490 | 7.53 | 1.82 | 6.05 |
| VitB12 or Folate | 16912 | 6.13 | 1.82 | 4.53 |
| HbA1c | 10768 | 10.25 | 1.82 | 6.10 |
| Rheuma factor | 3431 | 4.40 | 0.73 | 2.43 |
| Transferrin | 14472 | 3.60 | 0.91 | 3.03 |
| Total IgE | 1900 | 9.63 | 1.82 | 6.00 |
| RAST | 3460 | 15.07 | 1.82 | 6.02 |

In this model, the income for the tests that were run in large numbers was higher than the cost that they generated, e.g. a creatinine cost € 1.01 and generated an income of € 1.87. This was the case for all general clinical chemistry, haematology and coagulation assays and for some hormone assays, for 40 tests in total. For 16 tests, the costs were higher than the income, e.g. serology, glycohemoglobin, electrophoresis, IgE and RAST. For 3 of these 16 tests, the costs were more than double the income: HBs antibodies, HBs antigen and RAST. Figure 1 shows that tests performed in higher numbers have a better cost/income ratio.

**Figure 1: relationship between the cost/income ratio for the studied tests and the annual number of tests.**



## Impact of decreasing use of tests

### *Methods*

We calculated what the costs would be if the number of routine tests was reduced by 10, 20 and 30%.

The other parameters of the simulation are given in table 5. These parameters were set arbitrarily. The depreciation costs remained the same and the personnel and reagent costs were decreased but to a lesser extent than the number of tests as the number of calibrations and controls were assumed to remain the same. In the studied laboratory the costs for the building, electricity, etc. are proportional to the income, so this proportion remained unchanged in our hypotheses.

At the income side of the equation, the income per test was reduced in the same manner as the number of tests (e.g. -30% if the number of tests was reduced by 30%) and the forfaitary part was also reduced, but proportionally with the reduction in the number of tests. Given the structure of the Belgian reimbursement for laboratory tests (a cost per test and a forfaitary sum in function of the sum of the costs for the individual tests), it is impossible to calculate the impact of a test reduction in the forfaitary sum, because there are thousands of possibilities depending on the original list of tests and the tests that are deleted.

### *Results*

Table 5 shows that with a decreasing number of tests, the costs per test increase, while the income remains more or less stable. As was shown in the previous paragraph, most tests performed less than 18490 times a year had a cost that was higher than the income they generated in the studied lab. But, only one test shifts from profitable to money-losing.

**Table 5. Results of the calculation of the costs for a medical laboratory if the number of routine tests was reduced by 10, 20 and 30% and the number of other tests remained equal.**

| | Actual situation | Routine tests -10% | Routine tests - 20% | Routine tests - 30% |
|---|---|---|---|---|
| Personnel costs | Actual situation | - 5% | -10 % | -15% |
| Depreciation costs | Actual situation | No change | No change | No change |
| Reagent costs | Actual situation | - 3 % | - 7 % | -20 % |
| Costs for infrastructure | Actual situation | Unchanged | unchanged | unchanged |
| Median cost (€) | 2.33 | 2.45 | 2.58 | 2.67 |
| Median income (€) | 3.03 | 3.02 | 3.01 | 3.00 |
| Number of profitable tests | 40 | 39 | 39 | 39 |
| Number of money-losing tests | 16 | 17 | 17 | 17 |

### *Conclusion*

This simulation showed that a reduction in the number of tests increases the cost of an individual test, and that this increased cost is not accompanied by an increase in income for each test.

These data do indicate a trend, but they should be confirmed by data from other laboratories, preferably laboratories that serve mainly outpatients, as this calculation is very dependent on the structure of the laboratory and the mix of tests that is

performed, e.g. the studied laboratory performs many specialised tests, and the 56 studied analytes represent only 45.4% of the total number of tests.

## Impact of stepwise testing

In stepwise testing only a limited set of tests are requested in a patient initially, followed by investigating any abnormal result with additional tests on the same blood sample. But, laboratories may not be inclined to proceed with these stepwise testing strategies, as it is more costly to them and reduces profit. In this paragraph, the impact on costs and income of stepwise testing are explored using a specific example on anaemia.

### *A. Cost of an extra test requested by telephone on an existing sample*

#### METHODS

We asked for information from 3 laboratories, 2 serving GPs and outpatients and 1 hospital laboratory. Only 1 laboratory provided data.

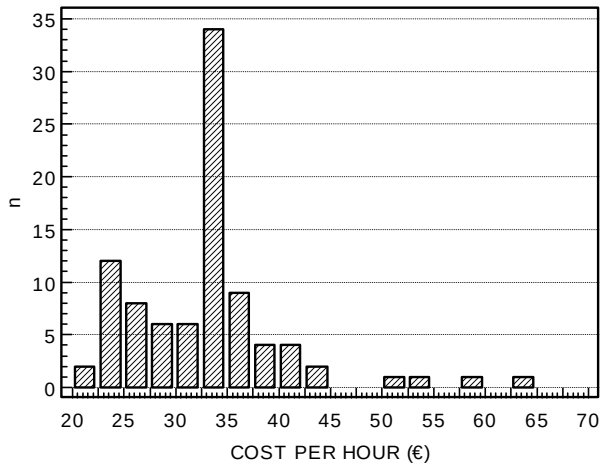
The extra time involved was calculated and multiplied with the average salary of a full-time laboratory technologist.

The average wages of a technologist were calculated from the total costs for 91 technologists in the laboratory that was studied for the other part of the economic analysis. Only 39 of them were full-time, so the wages were corrected in order to obtain the wage of a full-time technologist. The extra compensation for night and weekend work is also included in the wage cost.

It was estimated that technologists work 1710 hours/year (45 weeks x 38h/week), which is higher than other estimations, e.g. it is estimated that the Belgian worker works 1550 hours per year[b]; another calculation used 1626 hours[c]. The average yearly cost for wages was € 56320, or € 0.549 per minute. As older personnel tend to work more part-time, this could shift the average hourly wage higher if all part-times are calculated as full-times. A correction was made that took into account part-time workers and the average cost per minute was € 0.540. This number was used in the calculations. The distribution of the hourly costs is given in figure 2. No correction was made for the reduction in working hours for technologists older than 46 years, because it is only applicable if they are working in a hospital.

**Figure 2: distribution of the wage cost per hour for medical laboratory technologists (n = 91).**

The 10th percentile is € 24.06, the 90th percentile is € 40.34




[b] http://www.jobat.be/nl/info/redactie/belg_te_duur.aspx, accessed June 10, 2007

### RESULTS

Table 6 gives the detailed calculation of the cost for performing an extra test.

**Table 6: time needed for the processing of a telephonic request for an extra test**

| | Time needed in seconds | | |
|---|---|---|---|
| | Extra chemistry test | Extra haematology test | Extra haematology test requested on a different day |
| Duration of telephone call, retrieval of the information and communication to the technologist (seconds) | 135 | 135 | 135 |
| Retrieval of the sample from storage, analysis (seconds) | 175 | 90 | 240 |
| Validation of the result, printing of extra report (seconds) | 55 | 55 | 55 |
| Total (seconds) | 365 | 280 | 430 |
| Cost (€) | 3.29 | 2.52 | 3.87 |

For a chemistry test, an extra 6 minutes and 5 seconds were needed. The extra cost of an extra test is € 3.29.

For a haematology test, the extra cost is a little lower, because the instrument measures all the parameters, so the sample doesn't need to be retrieved, but the result must be retransferred to the laboratory information system. An extra cost of € 2.52 was calculated. If the request for an additional haematology assay comes on a later date, a date change must be made in the software, and the cost is € 3.87.

This cost is an additional cost, on top of the costs that are already made, e.g. reagents, and it is higher than the cost of most tests if performed on the original sample.

If more than one extra test is requested, the cost per test would be lower, but this depends on the number of sample types (EDTA-plasma, serum, …) and the number of instruments that are needed.

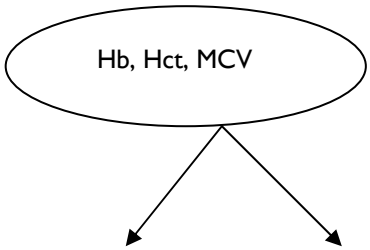
The possibility to use algorithms that are agreed upon by the laboratory and the requesting physician could reduce this cost if they can be programmed in the laboratory information system or in the instruments.

## *B. Case studies for stepwise testing*

### *i. Anaemia testing*

In the prospective study of chapter 5, Hb, Hct and MCV were ordered in 1018 cases or 64.5% of all orders. In 525 or 51.6 % of these cases, ferritin and/or vitamin B12/folate were ordered in the same order. Ferritin and vitamin B12/folate were ordered together in 68 cases. In 6 cases ferritin was ordered without Hb, Hct and MCV. In 61 cases vitamin B12/folate was ordered without Hb, HCT and MCV (figure 3).

[c] http://www.uzleuven.be/uzroot/hosting/labo/leermodule/eblm/EBLM_LM_CAT/2002-2003/Documenten/CAT_20030520_Helicobacter.pdf, accessed June 10, 2007. This study used a mean annual cost of € 43928 for medical laboratory technicians, which translated into a cost per minute of € 0.45.




493 (48.4%) 525 (51.6%)

| | | |
|---|---|---|
| not combined with ferritin or vitamin B12/folate | with ferritin : | 376 (72%) |
| | with vitamin B12 /folate : | 81 (15 %) |
| | with ferritin and vitamin B12/folate : | 68 (13%) |

**Figure 3: distribution of the combination of tests in the prospective study.**

But, as was shown in the chapter on guideline synthesis, the first step in patients suspected of anaemia is the measurement of Hb, Hct and MCV to confirm the presence of anaemia and if so, to classify the type of anaemia (macrocytic, microcytic, normocytic).

The results of these tests subsequently determine which test should be ordered next:

- ferritin in case of microcytic anaemia
- Vitamin B12 and folate (and other) in case of macrocytic anaemia.

Ordering Hb, Hct and MCV at the same time as vitamin B12 and/or folate is not recommended and there are no indications for ordering vitamin B12/folate and ferritin together.

## *Methods*

The costs and income for four different scenarios were simulated: (table 7)

1. all tests for anaemia are requested at once
2. only RBC/HCT and HGB are requested
3. RBC/HCT and HGB are requested and ferritin is requested later
4. RBC/HCT and HGB are requested and the tests for macrocytic anemia are requested later

For each scenario, the costs, income and B-value were brought in the simulation. For the income, the real reimbursement from the Belgian social security was used. In the Belgian nomenclature, each test is assigned a B value, the sum of which determines the forfaitary sum that is paid by the health insurance. For the first scenario the costs calculated in the previous subchapter were used, for the other scenarios, the cost was used based on a hypothesis of a reduction of 30% in the number of tests as outlined in the previous paragraph. For the sequential analysis, the extra cost calculated in table 6 was added to the costs. For scenario 4, as LDH and Vitamin B12 are performed on 2 different instruments an extra cost was added corresponding to 175 seconds of technologist work, or € 1.58. For haematology tests that are performed together on the instrument the cost corresponding to all the tests was used.

**Table 7: calculation of the B-values, income and cost for 3 scenarios for anemia testing.**

| Analyte | 1. RBC/HCT + HGB + B12/FA at once | | | 2. RBC/HCT + HGB | | | 3. RBC/HCT + HGB + ferritin | | | 4. RBC/HCT + HGB + B12/FA | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | B[1] | Income[2] (€) | Cost[3] (€) | B | Income (€) | Cost (€) | B | Income (€) | Cost (€) | B | Income (€) | Cost (€) |
| RBC/HCT | 40 | 0.29 | 4.59[4] | 40 | 0.29 | 5.61[6] | 40 | 0.29 | 5.61 | 40 | 0.29 | 5.61 |
| HGB | 40 | 0.29 | | 40 | 0.29 | | 40 | 0.29 | | 40 | 0.29 | |
| Ferritin | 250 | 1.82 | 7.53 | | | | 250 | 1.82 | 8.74 | | | |
| B12 & folate | 400 | 2.91 | 12.26[5] | | | | | | | 400 | 2.91 | 14.22 |
| Retics | 70 | 0.51 | | | | | | | | 70 | 0.51 | |
| WBC | 40 | 0.29 | | | | | | | | 40 | 0.29 | |
| Platelets | 40 | 0.29 | | | | | | | | 40 | 0.29 | |
| LDH | 80 | 0.58 | 1.15 | | | | | | | 80 | 0.58 | 1.30 |
| Extra cost for telephonic add-on request | | | | | | | | | 3.29 | | | 7.39[7] |
| Sum | 960 | 6.98 | 25.53 | 80 | 0.58 | 5.61 | 330 | 2.4 | 17.64 | 710 | 5.16 | 28.52 |
| Fixed income/sample | | 32.37 | | | 19.99 | | | 19.99 | | | 32.37 | |
| Total income | | 39.35 | | | 20.57 | | | 22.39 | | | 37.53 | |
| Profit | | 13.82 | | | 14.96 | | | 4.75 | | | 9.01 | |

[1] The B-value is how the health insurance calculates the reimbursement. B= 25% of € 0.029093, or € 0.0073; the total sum of the B values determines which forfaitary sum is paid for the entire request.

[2] Income based on the official social security tariff

[3] Cost based on the values in table 4

[4] As a haematology analyser measures all parameters at once, the cost for running one parameter is the sum of the cost of hemoglobin, RBC/HCT, reticulocytes, WBC and thrombocytes or € 0.81+0.84+1.28+0.83+0.83= € 4.59

[5] The cost was calculated for B12 or folate; if both are requested, the cost is 2 x € 6.13 or € 12.26

[6] In this and the other scenarios, the number of tests performed by the laboratory is lower, so the cost calculated in our hypothesis of a reduction with 30% was used.

[7] For scenario 4, as LDH and Vitamin B12 are performed on 2 different instruments an extra cost for a telephonic request was added corresponding to 175 s of technologist work, see table 6: € 3.29 for an extra chemistry test, € 2.52 for an extra haematology test and € 1.58 for the chemistry test on an extra analyser.

For the first scenario the costs calculated in the previous subchapter were used, for the other scenarios, the cost was used based on a hypothesis of a reduction of 30% in the number of tests. For sequential analysis, the extra cost calculated above was used. For haematology tests that are determined together on the instrument the cost corresponding to all the tests was used. For the income, the real reimbursement from the Belgian social security was used.

The total costs of a stepwise testing strategy further depend on the proportion of the different strategies. Iron deficiency anaemia is more prevalent than vitamin B12 and folate deficiency anaemia. According to data from a morbidity registration in the Netherlands, the incidence of 'iron deficiency anaemia' in general practice is 11.5/1000 women/yr and 7.3 men/1000 men/year. The incidence of 'anaemia, vitamin B 12 and folate deficiency' is 0.8/1000 women/year and 0.5/1000 men/year. The incidence of 'anaemia/not specified' is 1.8/1000 men/year and 2.4/1000 women/year (Okkes IM, Oskam SK, Lamberts H. Van klacht tot diagnose; Episodegegevens uit de huisartspraktijk. Coutinho, Bussum, Nl. 1998).

If we apply the proportion of males/females found in the prospective study (44.7/55.3) the incidence becomes 9.2 patients/1000/year with iron deficient anaemia and 0.63/1000/year vitamin B12 and folate deficient anaemia respectively.

We also hypothesized that the general practitioner did not take blood in 100% of his patients, but in 10% (1994 data mentioned in the introduction of the report). It follows that the stepwise testing would result in a limited request in each patient suspected of anaemia (n=100), an additional request of ferritin in 9 patients and an additional request for vitamin deficient and other causes in 1 patient.

Table 8 shows the calculations for two alternatives:

1. all tests are requested at once on 100 samples
2. only RBC/HCT and HGB are requested in 90 samples and ferritin and the macrocytic anaemia panel are requested in 9 and 1 patients respectively

**Table 8: Calculation of the incomes and costs for the two alternatives in test requesting for anaemia**

| Alternative | n | scenario | income | cost | Profit |
|---|---|---|---|---|---|
| 1 | 100 | 1 | 39.35 | 25.53 | |
| | 0 | 2 | 20.57 | 5.61 | |
| | 0 | 3 | 22.39 | 17.64 | |
| | 0 | 4 | 37.53 | 28.52 | |
| | | | | | |
| | Total | | 3935.00 | 2553.00 | 1382.00 |
| | | | | | |
| 2 | 0 | 1 | 39.35 | 25.53 | |
| | 90 | 2 | 20.57 | 5.61 | |
| | 9 | 3 | 22.39 | 17.64 | |
| | 1 | 4 | 37.53 | 28.52 | |
| | | | | | |
| | Total | | 2090.34 | 692.18 | 1398.16 |

From table 8 it appears that sequential requesting taking into account a higher cost per test and the extra cost for sequential testing, results in a decrease in turnover but an equal profit for the medical laboratory.

This conclusion is explained by the fact that the current reimbursement system favours small requests, because a large fixed sum per request is added to the low reimbursement per test. But the prospective study has shown that general practitioners often consider different hypotheses for a diagnosis, so often more tests will be requested.

However this calculation is based on the data from only one laboratory that is large and hospital-based. Data from more laboratories are needed before one can conclude that requesting along the guidelines does not result in decreasing profits for the laboratories in ambulatory care.

### II. THYROID TESTING

A second example is based on screening for thyroid disorders (see 4.4.55).

The guidelines recommend screening for TSH, and performing a FT4 if TSH is raised and a FT3 is TSH is low.

In the prospective study, 42% of the requests were for TSH alone, 15% for TSH with FT4 and 5% for TSH, FT4 and FT3. Six different scenarios were considered: TSH+FT4+FT3 at once, TSH and FT4 at once, TSH and FT3 at once, TSH only, TSH and FT4 if TSH raised, and finally TSH and FT3 if TSH is low.

The calculation for the income and costs of 6 scenarios is given in table 9.

**Table 9: calculation of the B-values, income and cost for 6 scenarios for thyroid disorders.**

| | 1. TSH + FT4 + FT3 at once | | | 2. TSH and FT4 at once | | | 3. TSH and FT3 at once | | |
|---|---|---|---|---|---|---|---|---|---|
| Analysis | B | Income | Cost | B | Income | Cost | B | Income | Cost |
| TSH | 250 | 1.82 | 4.17 | 250 | 1.82 | 4.5[1] | 250 | 1.82 | 4.5 |
| FT4 | 350 | 2.55 | 5.77 | 350 | 2.55 | 6.22 | | | |
| FT3 | 350 | 2.55 | 6.44 | | | | 350 | 2.55 | 6.95 |
| Sum | 950[2] | 6.92[2] | 16.38 | 600 | 4.37 | 10.72 | 600 | 4.37 | 11.45 |
| Fixed income/sample | | 32.37[2] | | | 19.99 | | | 19.99 | |
| Total income | | 39.29 | | | 24.36 | | | 24.36 | |
| Profit | | 22.91 | | | 13.64 | | | 12.91 | |
| | 4. TSH only | | | 5. TSH and FT4 if raised | | | 6. TSH and FT3 if low TSH | | |
| Analysis | B | Income | Cost | B | Income | Cost | B | Income | Cost |
| TSH | 250 | 1.82 | 4.5 | 250 | 1.82 | 4.5 | 250 | 1.82 | 4.5 |
| FT4 | | | | 350 | 2.55 | 6.22 | | | |
| FT3 | | | | | | | 350 | 2.55 | 6.95 |
| Extra cost for add-on request | | | | | | 3.29 | | | 3.29 |
| Sum | 250 | 1.82 | 4.5 | 600 | 4.37 | 14.01 | 600 | 4.37 | 14.74 |
| Fixed income/sample | | 19.99 | | | 19.99 | | | 19.99 | |
| Total income | | 21.81 | | | 24.36 | | | 24.36 | |
| Profit | | 17.31 | | | 10.35 | | | 9.62 | |

[1]Higher cost per tests because of a lower number of tests performed in the lab

[2]The social security reimburses 3 thyroid tests only if one was abnormal. The calculation was made according to this scenario. If this assumption was not made, the income for scenario 1 would be € 1.82 less.

Table 10 calculates the total cost for the current situation (alternative 1), if the stepwise testing according to the guidelines were followed (alternative 2) and if the three tests were ordered at once (alternative 3). The incidence of hypothyroidism has been found to be 4.1/1000/year in women and 0.6/1000/year in men. The incidence of hyperthyroidism was 0.8/1000/year and negligible in men (Vanderpump 1995). Considering laboratory tests for thyroid function are requested in patients with signs and symptoms suggestive of those disorders, the incidence of thyroid disorders in the tested population would be expected to be higher. A survey of 57830 TSH results from an outpatient laboratory showed that 10.5% of the results were abnormal (5.8% too low and 4.7% too high). Based on these data we considered that 4 and 3 out of the 62 cases would have a low and a high TSH respectively.

**Table 10: Calculation of the incomes and costs for the three alternatives in test requesting for thyroid disorders**

| Alternative | scenario | n | income | cost | Profit |
|---|---|---|---|---|---|
| 1 Current situation | 1 | 5 | 39.29 | 16.38 | |
| | 2 | 15 | 24.36 | 10.72 | |
| | 3 | 0 | 24.36 | 11.45 | |
| | 4 | 42 | 21.81 | 4.50 | |
| | 5 | 0 | 24.36 | 14.01 | |
| | 6 | 0 | 24.36 | 14.74 | |
| | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| | Total | 62 | 1477.87 | 431.70 | 1046.17 |
| | scenario | n | income | cost | Profit |
| 2 Following guidelines | 1 | 0 | 39.29 | 16.38 | |
| | 2 | 0 | 24.36 | 10.72 | |
| | 3 | 0 | 24.36 | 11.45 | |
| | 4 | 55 | 21.81 | 4.50 | |
| | 5 | 3 | 24.36 | 14.01 | |
| | 6 | 4 | 24.36 | 14.74 | |
| | | | | | |
| | Total | 62 | 1370.07 | 348.49 | 1021.58 |
| | scenario | n | income | cost | Profit |
| 3 3 test ordered at once | 1 | 7 | 39.29[1] | 16.38 | |
| | 1' | 55 | 37.47[1] | 16.38 | |
| | 2 | 0 | 24.36 | 10.72 | |
| | 3 | 0 | 24.36 | 11.45 | |
| | 4 | 0 | 21.81 | 4.50 | |
| | 5 | 0 | 24.36 | 14.01 | |
| | 6 | 0 | 24.36 | 14.74 | |
| | | | | | |
| | Total | 62 | 2335.88 | 1015.56 | 1320.32 |

[1]Based on the reimbursement rules, only two thyroid tests would be reimbursed if the three tests are normal. In that case, the income would be € 37.47. In the calculation of the profit, we considered that 6 samples (10%) would have at least one abnormal thyroid test.

In this case, stepwise requesting according to the guidelines causes a small reduction in income and profit for the laboratories: the income is reduced by 8% and the profit by 2%. But, this algorithm can be performed by the laboratory automatically, as no input of the treating physician is necessary. Therefore, the costs of the additional tests are probably overrated in this simulation. If the three thyroid tests are requested at once, this is much more costly (+70%) for the social security, while the profit is approximately 29% higher than when the guidelines are followed.

# GLOSSARY

- APTT: partial thromboplastin time. It is used as a screening test and to monitor heparin therapy.
- ALT: alanine transaminase; An enzyme that catalyzes the conversion of L-alanine and 2-oxoglutarate to pyruvate and L-glutamate. The older name GPT (Glutamic Pyruvic Transaminase) is still commonly used.
- AST: Aspartate Aminotransferase. Enzymes of the transferase class that catalyze the conversion of L-aspartate and 2-ketoglutarate to oxaloacetate and L-glutamate. The older name GOT (Glutamic Oxaloacetic Transaminase) is still commonly used.
- CA-15-3 antigen: Carbohydrate antigen elevated in patients with tumors of the breast, ovary, lung, and prostate as well as other disorders.
- CA-19-9 antigen: Sialylated Lewis blood group carbohydrate antigen found in many adenocarcinomas of the digestive tract, especially pancreatic tumors.
- CEA: carcinoembryonic antigen A glycoprotein that is secreted into the luminal surface of the epithelia in the gastrointestinal tract.
- GGT: gamma-glutamyltransferase; An enzyme, sometimes called GGT, with a key role in the synthesis and degradation of glutathione.
- Glycohemoglobin, Hemoglobin A, Glycosylated Hemoglobin A1c is most important. The concentration of glycosylated hemoglobin A is a more reliable index of the blood sugar average over a long period of time.
- LDH: L-lactate dehydrogenase. A tetrameric enzyme that, along with the coenzyme NAD+, catalyzes the interconversion of lactate and pyruvate.
- RAST: Radioallergosorbent Test; An in vitro allergen radioimmunoassay in which allergens are coupled to an immunosorbent. The coupled allergens bind the IgE in the sera of patients which in turn binds radioisotope-labeled anti-immunoglobulin E antibodies
- TPHA/TPPA: Treponema pallidum haemagglutination assay; Treponema pallidum Particle Agglutination Testing.
- VDRL/RPR: Venereal Disease Research Laboratory test (VDRL) is a nontreponemal serological screening for syphilis. Rapid plasma reagin (RPR) test. The RPR test also detects syphilis antibodies.

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Wettelijk depot : D/2007/10.273/24

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