

Analyses de biologie clinique en médecine générale

KCE reports 59B

Le Centre fédéral d'expertise des soins de santé

Présentation : Le Centre fédéral d'expertise des soins de santé est un parastatal, créé le 24 décembre 2002 par la loi-programme (articles 262 à 266), sous tutelle du Ministre de la Santé publique et des Affaires sociales, qui est chargé de réaliser des études éclairant la décision politique dans le domaine des soins de santé et de l'assurance maladie.

Conseil d'administration

Membres effectifs : Gillet Pierre (Président), Cuypers Dirk (Vice-Président), Avontroodt Yolande, De Cock Jo (Vice-Président), De Meyere Frank, De Ridder Henri, Gillet Jean-Bernard, Godin Jean-Noël, Goyens Floris, Kesteloot Katrien, Maes Jef, Mertens Pascal, Mertens Raf, Moens Marc, Perl François Smiets, Pierre, Van Massenhove Frank, Vandermeeren Philippe, Verertbruggen Patrick, Vermeyen Karel.

Membres suppléants : Annemans Lieven, Boonen Carine, Collin Benoît, Cuypers Rita, Dercq Jean-Paul, Désir Daniel, Lemye Roland, Palsterman Paul, Ponce Annick, Pirlot Viviane, Praet Jean-Claude, Remacle Anne, Schoonjans Chris, Schrooten Renaat, Vanderstappen Anne.

Commissaire du gouvernement : Roger Yves

Direction

Directeur général : Dirk Ramaekers

Directeur général adjoint : Jean-Pierre Closon

Contact

Centre fédéral d'expertise des soins de santé (KCE).
Rue de la Loi 62
B-1040 Bruxelles
Belgium

Tel: +32 [0]2 287 33 88

Fax: +32 [0]2 287 33 85

Email : info@kce.fgov.be

Web : <http://www.kce.fgov.be>

Analyses de biologie clinique en médecine générale

KCE reports 59B

AN DE SUTTER, ANN VAN DEN BRUEL, STEPHAN DEVRIESE, FRANÇOISE MAMBOURG,
VÉRONIQUE VAN GAEVER, ALAIN VERSTRAETE, MICHEL HUYBRECHTS

KCE reports 59B

Titre : Analyses de biologie clinique en médecine générale

Auteurs : An De Sutter (UGent), Ann Van den Bruel (KCE), Stephan Devriese (KCE), Françoise Mambourg (KCE), Véronique Van Gaever (UGent), Alain Verstraete (UGent), Michel Huybrechts (KCE).

Experts externes: Norbert Blanckaert (KULeuven), Etienne Vermeire (UA), Nerée Claes (Universiteit Hasselt), Piet Vandebussche (Domus Medica), Daniel Burdet (Maisons Medicales), Geert-Jan Dinant (Universiteit Maastricht, Nederland).

Validateurs: Ron Winkens (Universiteit Maastricht, Nederland), Britt Van Meensel (KULeuven), Philippe Michielsens .

Conflict of interest : Aucun conflit déclaré.

Disclaimer: Les experts externes et validateurs ont collaboré à la rédaction du rapport scientifique mais ne sont pas responsables des recommandations aux Autorités. Les recommandations aux Autorités ont été rédigées par le Centre d'expertise (KCE).

Mise en Page : Nadia Bonnouh, Ine Verhulst.

Bruxelles, juillet 2007

Etude nr 2006-01

Domaine : Good Clinical Practice (GCP)

MeSH : Laboratory Techniques and Procedures, Family Practice, Quality of Health, Care

NLM classification : QY 25

Langage : français, anglais

Format : Adobe® PDF™ (A4)

Dépôt légal : D/2006/10.273/25

La reproduction partielle de ce document est autorisée à condition que la source soit mentionnée. Ce document est disponible en téléchargement sur le site Web du Centre fédéral d'expertise des soins de santé.

Comment citer ce rapport ?

De Sutter A., Van den Bruel A., Devriese S., Mambourg F., Van Gaever V., Verstraete A., Huybrechts M. Analyses de biologie clinique en médecine générale. Good Clinical Practice (GCP). Bruxelles: Centre fédéral d'expertise des soins de santé (KCE); 2007. KCE reports 59B (D/2006/10.273/25).

PRÉFACE

De nos jours, il n'est plus possible d'exercer la médecine sans recourir aux analyses de laboratoire. La plupart de celles-ci permettent une avancée importante dans la détermination du diagnostic et dans le suivi des maladies et de leur traitement. C'est pour cette raison que leur utilisation n'a cessé de croître au cours des dernières décennies.

Toutefois, il n'est pas toujours aisé pour le médecin de faire un choix parmi les nombreux tests proposés et de définir au mieux l'indication précise de chacun d'entre eux. Le fait de réaliser des analyses non indispensables peut exposer le patient à des conséquences néfastes. En effet, des résultats faussement positifs induisent le risque de réaliser d'autres tests et/ou des traitements inadéquats, et des études antérieures ont démontré que l'utilisation de tests non indispensables diminue la satisfaction des patients. Par opposition à cela, il arrive que certaines analyses soient sous-utilisées, avec comme conséquence, une dispensation sub-optimale des soins.

Le coût unitaire d'une analyse n'est pas élevé, cependant leur coût total est considérable. A l'époque où les besoins de santé augmentent, la nécessité d'une utilisation efficace des moyens s'accroît elle aussi. Il n'existe actuellement que peu de stimuli destinés à encourager les prescripteurs à l'utilisation rationnelle des analyses. Une lettre de la Commission de Biologie Clinique (SPF, Santé Publique) a interpellé récemment certains laboratoires (ceux qui accordent des avantages substantiels aux prescripteurs) pour leur rappeler que certains avantages ne peuvent être considérés comme un cadeau de fidélisation « normal ».

La réalisation de ce rapport a nécessité la collecte de demandes d'analyses de laboratoire afin de permettre leur étude détaillée : nous tenons à remercier ici les nombreux biologistes et médecins généralistes sans qui ce travail aurait été impossible. De plus, ce rapport a été l'occasion d'étudier les interventions envisageables dans le but d'optimiser le comportement prescripteur. Enfin, ce rapport tente également d'évaluer si l'habitude des patients de réclamer « une prise de sang » pour toutes leurs plaintes se justifie.

Jean-Pierre CLOSON
Directeur général adjoint

Dirk RAMAEKERS
Directeur général

EXECUTIVE SUMMARY

INTRODUCTION

L'objectif principal de ce rapport consiste à évaluer si les analyses de biologie clinique sont utilisées de manière appropriée en médecine générale et à investiguer les méthodes utilisables pour améliorer le comportement prescripteur.

DESCRIPTION GÉNÉRALE

D'une manière générale, l'utilisation des tests de biologie clinique s'accroît bien que ce soit l'inverse pour quelques tests. Ce sont les tests de coagulation qui augmentent relativement le plus, passant de 1.500.000 tests par an en 1995 à plus de 3.500.000 en 2005.

Les patients qui prennent des médicaments pendant plus de trois mois par an sont soumis plus souvent à des analyses, l'intervalle moyen étant pour eux de 3.9 mois entre les analyses et de 6.6 mois pour les autres patients. On relève la même tendance à la répétition des analyses pour les patients qui viennent d'être hospitalisés plusieurs jours. Toutefois, ces différences ne sont pas très importantes.

UTILISATION APPROPRIÉE DES ANALYSES EN MÉDECINE GÉNÉRALE

DÉFINITION

La revue de littérature a mis 317 articles en évidence. Il n'en restait que neuf après application des critères d'inclusion et d'exclusion. Quatre d'entre eux se basent sur des recommandations issues de guidelines pour juger si la réalisation de l'analyse est appropriée. Deux d'entre se basent sur des opinions d'experts. Un article se base sur les données probantes spécifiques aux caractéristiques de l'analyse pour juger de son caractère approprié; les deux derniers articles ne définissent pas leurs critères de jugement, bien que l'un deux présente un algorithme décisionnel pour les tests thyroïdiens.

Pour conclure, les recommandations issues de guidelines ont été considérées comme la manière la plus appropriée de juger de l'adéquation d'une analyse.

SYNTHÈSE DES GUIDELINES EXISTANTS

Les guidelines et recommandations de bonne pratique relatifs aux analyses de biologie clinique ont été recherchés et synthétisés. Cela représente 118 guidelines au total. La plupart d'entre eux ont pour objet une maladie et ne contiennent que quelques paragraphes au sujet des tests. Un seul d'entre eux, à savoir le guideline du Nederlands Huisartsen Genootschap (NHG) développé en collaboration avec le National College of Clinical Chemists and the Collaboration of Laboratories, se réfère spécialement aux analyses biologiques en médecine générale.

Le dosage de l'hémoglobine est recommandé pour 35 indications différentes et la créatinine pour 22. Le glucose arrive en troisième place avec 18 indications. Quelques tests, comme le dosage du chlore et du fibrinogène qui sont pourtant utilisés régulièrement dans la pratique belge ne sont pas recommandés dans plusieurs guidelines.

Seules 24 indications rapportées par les guidelines se réfèrent à des niveaux de preuve ou à des niveaux de recommandation. Aucune autre indication ne dispose de référence que ce soit à un niveau de preuve qui puisse justifier une recommandation ou à un niveau de recommandation qui aurait pu en découler.

ÉTUDE PROSPECTIVE EN MÉDECINE GÉNÉRALE

Cent soixante quatre médecins généralistes ont, en collaboration avec cinq laboratoires privés, participé à l'étude qui a permis d'étudier 1.579 demandes d'analyse. Les médecins ont été interrogés sur la motivation principale de la prise de sang et sur les raisons particulières de demander chaque test (ex : exclure une maladie, confirmer un diagnostic, répondre à la demande d'un patient, etc)

L'âge moyen des patients était de 58.2 ans (SD 20.1) dont 44.7% d'hommes. En moyenne, 13.3 tests étaient demandés par analyse. Le coût moyen d'une analyse s'élevait à 39.4€ dont 7.3€ à charge du patient. Le dosage du PTT/INR figurait dans 18% des demandes. Si on fait exception des dosages du PTT/INR, le nombre moyen de tests par analyse était de 16, ce qui représente un coût total de 44.1€ dont 9.1€ à charge du patient.

Les dix analyses les plus fréquentes étaient : Hémoglobine, Hématocrite+comptage des érythrocytes, globules blancs, formule, TGO+TGP, créatinine, glucose, plaquettes, gamma-GT et cholestérol total.

La motivation principale de la prise de sang elle-même était le follow-up d'une affection chronique ou d'un traitement (55%). Dans 20%, il s'agissait d'établir un diagnostic et dans 10%, d'effectuer un check-up ou de déterminer des paramètres en prévention. On retrouvait aussi dans une moindre mesure, les demandes induites par le patient (4%) et les demandes induites par le spécialiste (0.4%). En plus de ces motifs principaux, les médecins ont spécifié d'autres raisons additionnelles dans près de 45% des cas : une raison additionnelle dans 34%, deux dans 9.4% et trois dans 22 situations.

Une analyse détaillée des motivations principales : check-up ou prévention générale, diabète, hypertension ou faiblesse/fatigue est présentée en détails dans le tableau 1 ci-dessous. La fréquence du problème en tant que motivation unique (colonne 2), la fréquence des motifs additionnels éventuels (colonne 3) ainsi que le nombre de tests prescrits (colonne 4) sont détaillés pour chaque item. Ensuite, le nombre de tests recommandés (colonne 5) par les guidelines est mentionné. Etant donné que ce nombre varie selon que l'on prend en compte uniquement la motivation principale ou également, les motivations additionnelles, un minimum et un maximum sont mentionnés. La proportion de tests non recommandés est calculée une première fois en fonction de la motivation principale et des motifs additionnels (colonne 6) et une deuxième fois en tenant compte d'autres raisons individuelles spécifiques au patient et déclarées par les médecins (colonne 7).

L'analyse financière détaillée en fonction des motivations principales figure au tableau 2 qui reprend : le coût total de toutes les prescriptions, le coût par prescription et la contribution du patient. Ensuite, le coût des tests recommandés par les guidelines pour l'indication principale est mentionné (scénario minimal). Ce coût est également recalculé en tenant compte des raisons secondaires (scénario maximal) et enfin ce coût est calculé en tenant compte des raisons secondaires et d'autres motivations spécifiques au patient déclarées par les médecins.

Enfin certains tests qui sont prescrits régulièrement mais peu souvent cités dans les guidelines, sont analysés en détails dans le tableau 3 en suivant la logique du tableau 1.

Tableau I: Motivation de prescription d'analyse de laboratoire en comparaison aux guidelines

	N de demandes	Presc Pour 1 motif principal %	Presc Pour plusieurs motifs %	Nombre de tests N (SD)	Tests recommandés n	Tests non recommandés %	Tests inappropriés %
Check-up/prévention	155	16	54% follow-up 25% demande patient 10% diagnostic	21 (6.1)	6-14	46	38
Diabète non insulín dépendant	205	17	76% follow-up 11% diagnostic 12% monitoring thérapeutique	13.5 (9.2)	9-18	62.1	39.8
Hypertension	184	11	76% follow-up 17% diagnostic 7% monitoring thérapeutique	17.2 (8.1)	8-12	66	59.6
Fatigue/faiblesse générale	121	0	25% follow-up 54% diagnostic 10% demande patient	19 (6.9)	6	74	44

Tableau 2: Analyse financière

	Coût total €	Coût/demande € (SD)	Coût patient € (SD)	Coût/demande tests recommandés €	Coût/demande tests Recommandés et additionnels €	Coût/demande tests Recommandés ,additionnels et spécifiques au patient €
Check-up/prévention	7770	50 (8)	11.5 (2.6)	24.4	41.6	44.3
Diabète non insulino dépendant	6897	45.4	7.1 (5.4)	40.4	42.6	43.4
Hypertension	8759	47.6 (12.7)	9 (5)	24.2	41.4	42.4
Fatigue/faiblesse générale	5985	49.4 (9.5)	11 (23.4)	24.4	24.4	41.3

Tableau 3: Tests particuliers

	Fréquence %	Raisons principales	Raisons spécifiques	Proportion de demandes inappropriées %
Urée	25.3	40% follow-up 26% diagnostic	50% screening 40% raisons cliniques: affection des reins, diabète en monitoring thérapeutique (diurétique)	87
Protéines totales	17.5	33% follow-up 29% diagnostic 29% check-up/prévention	70% screening 19% diagnostic: inflammation et déficience nutritionnelle	100
Amylase	13.7	31% follow-up 29% diagnostic 26% check-up/prévention	70% screening 26% diagnostic: pancréas ou abus chronique d'alcool	77.5
Plaquettes	52.8	38% follow-up 28% diagnostic 16% check-up/prévention	80% screening 7% monitoring thérapeutique ou diagnostic	95
Chlore	16.7	42% follow-up 23% diagnostic 20% check-up/prévention	42% screening 43% monitoring thérapeutique ou diagnostique (désordres électrolytes)	100

INTERVENTIONS DESTINÉES A MODIFIER LE COMPORTEMENT PRESCRIPTEUR

La recherche de littérature a permis d'identifier une revue systématique de qualité satisfaisante qui a été complétée par 12 études originales.

La revue systématique fait état d'une diminution ou d'un changement des analyses prescrites dans 76% des études répertoriées. Les interventions qui influencent plusieurs facteurs comportementaux sont plus fréquemment (86% de réussite) couronnées de succès que celles qui ne visent qu'un facteur à la fois (62% de réussite). Les interventions combinaient diverses stratégies : groupes de pairs, audit et feedback, dissémination des recommandations, messages de type « reminders », demande de justification (de certaines prescriptions), modification de la forme de la demande d'analyse.

Implémentation des recommandations et feedbacks

Deux études ont évalué une stratégie qui utilisait les recommandations comme base des feedbacks. L'une d'elle n'a pas mis en évidence d'effet sur le nombre de tests demandés, tandis que l'autre a démontré une diminution de 5%.

Un essai contrôlé randomisé a évalué dans trois groupes distincts l'efficacité de la discussion par des médecins généralistes de feedbacks de leurs demandes d'analyses comparées à trois recommandations basées sur les données probantes (EBM-based). Une diminution (12%) significative ($p < 0.05$) du nombre de tests demandés a été observée dans un des groupes, tandis qu'une diminution non significative (8% versus 3% dans le groupe de contrôle) était enregistrée dans le deuxième.

Dans un autre essai contrôlé randomisé en grappes consistant en un feedback accompagné ou non de messages de type « reminders », le groupe d'intervention a prescrit significativement moins que le groupe de contrôle : le rapport de cotes pour le groupe feedback était de 0.87 (95%CI 0.81 - 0.94), celui du groupe « reminders » de 0.89 (95%CI 0.83 - 0.93), et celui du groupe ayant bénéficié de la combinaison du feedback et des « reminders » était de 0.78 (95%CI 0.71 - 0.85).

Une intervention de longue durée (9 années) effectuée à Maastricht (Pays-Bas) a consisté en l'envoi répété tous les six mois de feedbacks personnels (basés sur les recommandations) et a permis de démontrer entre 1984 et 1993 une diminution de 45% des prescriptions de 44 tests classiques (diminution annuelle moyenne de 6%, $p < 0.001$) dans le groupe participant. Le groupe de contrôle a quant à lui montré une augmentation annuelle de 3.2%.

Aide à la décision assistée par ordinateur

Un essai contrôlé randomisé a comparé l'efficacité de deux interventions axées sur l'utilisation d'un ordinateur. Un des groupes a utilisé simplement une demande d'analyse restreinte (ne comportant que certains tests), tandis que l'autre a utilisé une version basée sur les recommandations. Ce dernier groupe a prescrit 20% en moins que l'autre ($p < 0.003$)

Modification de la forme de la prescription

Dans un essai contrôlé randomisé, le nombre de test demandés a diminué de 18% après l'introduction d'un formulaire de demande d'analyse comportant une liste réduite, mais cette diminution ne s'est pas maintenue après réintroduction de la liste habituelle ($p < 0.001$). Smithuis a également obtenu une diminution significative de la prescription de 3 tests (sur un total de 6), en utilisant une liste abrégée. Dans une étude avant-après, l'utilisation d'une liste abrégée accompagnée d'un feedback réalisé tous les 6 mois, a abouti à une réduction de 23% des tests prescrits. Des résultats similaires ont été obtenus au Royaume-Uni par Bailey et son équipe.

Interventions financières

Une étude canadienne rétrospective a permis de comparer trois interventions combinées: l'utilisation de recommandations, la modification de la liste et le changement de certains remboursements (arrêt du remboursement du dosage de thyroxine). Cette étude a montré une diminution de 58% du dosage de l'urée et de 80% de celui du fer sérique.

Pour un essai réalisé en Nouvelle-Zélande, les généralistes ont eu la possibilité d'allouer le gain financier réalisé en diminuant le nombre d'analyses de laboratoire, à d'autres aspects de leur pratique clinique. Cette intervention a permis une économie globale de 22.7% des coûts de laboratoire pour une période de 13 mois. Toutefois, si le groupe d'intervention réalisait une économie de 32.9%, le groupe de contrôle en réalisait également une de 20.3%.

DISCUSSION

Les analyses de laboratoire sont prescrites de plus en plus fréquemment en médecine générale, bien que cette augmentation ne soit pas uniforme et que certains tests soient au contraire moins utilisés. Les recommandations de bonne pratique sont considérées comme la base la plus appropriée pour juger de l'adéquation d'un test. Toutefois, ces recommandations ne sont pas toujours concordantes et il est rare que les niveaux d'évidence soient mentionnés.

Il est fréquent que les médecins généralistes prescrivent des analyses de biologie clinique pour plusieurs raisons à la fois. Ceci amène une grande incertitude quant à la pertinence du test demandé, même si de nombreux tests peuvent être considérés comme inappropriés. D'un autre côté, il est fréquent que des tests pourtant recommandables ne fassent pas partie des demandes. Ceci démontre que les interventions conçues dans le but de modifier le comportement prescripteur ne devraient pas se focaliser uniquement sur une diminution du nombre total d'analyses, mais bien viser à améliorer la qualité.

L'étude de la littérature démontre que des interventions telles que les audits, les feedbacks, les prises de décision assistées par ordinateur peuvent être utiles pour modifier le comportement des prescripteurs dans ce domaine. Toutefois, ces interventions gagnent à être bien conçues et organisées, à être basées sur les recommandations, à faire partie d'un processus continu et à être adaptées au contexte local. Le coût d'une intervention peut s'avérer moins élevé que les économies réalisées, comme cela a été démontré par Poley. Dans sa recherche, les coûts totaux d'intervention s'élèvent à 670€ pour une pratique tandis que les économies réalisées se chiffrent à 847€ par pratique tous les six mois.

CONCLUSIONS ET RECOMMANDATIONS AUX DECIDEURS

- Il est nécessaire que les médecins généralistes disposent d'une information indépendante relative à l'utilisation appropriée des analyses de laboratoire, valide au niveau scientifique et aisément accessible.
- Il est nécessaire qu'une telle recommandation soit élaborée au niveau national en collaboration avec l'association des cliniciens biologistes afin d'être mise à la disposition des médecins généralistes. Les aspects pre-analytiques doivent ainsi être inclus. Une telle recommandation devrait constituer une priorité pour les organisations scientifiques de médecins généralistes. Une collaboration avec les biologistes cliniques est souhaitable.
- L'intégration de cette information à la pratique quotidienne est indispensable. Cette intégration pourrait être réalisée au moyen de feedbacks développés au départ de la recommandation nationale et qui seraient répétés.
- L'utilisation d'un formulaire de demande d'analyse comportant une liste de tests réduite devrait permettre de diminuer la prescription des tests inappropriés et accroître la prescription de ceux qui le sont. Cette liste couplée à une aide à la décision assistée par ordinateur pourrait être intégrée dans les logiciels de gestion du dossier médical.
- Il est souhaitable que l'information relative aux coûts des tests de laboratoire (pour l'assurance maladie comme pour le patient) soit plus facilement accessible. Les logiciels de gestion du dossier médical en médecine générale pourraient également être programmés pour afficher ces coûts.

Scientific summary

Table of contents

1	INTRODUCTION	5
2	THE USE OF LABORATORY TESTS IN BELGIUM	6
2.1	INTRODUCTION	6
2.2	METHODOLOGY	6
2.3	RESULTS.....	9
2.3.1	RIZIV/INAMI data on nomenclature use.....	9
2.3.2	Intermutualistisch agentschap (IMA) data	11
3	APPROPRIATE USE OF LABORATORY TESTS IN GENERAL PRACTICE.....	16
3.1	INTRODUCTION	16
3.2	METHODS.....	16
3.3	RESULTS	17
3.4	DISCUSSION	17
4	SYNTHESIS OF EXISTING GUIDELINES	19
4.1	INTRODUCTION	19
4.2	METHODS.....	19
4.3	RESULTS.....	19
4.4	RECOMMENDATIONS PER INDICATION	20
4.4.1	Hyperhidrosis, ICPC code A09.....	20
4.4.2	Suspicion of infectious mononucleosis, ICPC code A75	20
4.4.3	Adverse effect of a therapeutic drug.....	20
4.4.4	Hypersensitivity, ICPC code A92	21
4.4.5	General check-up/vague complaints, ICPC code A98.....	21
4.4.6	Statin therapy, ICPC code B34.....	21
4.4.7	Heparin therapy, ICPC code B34	22
4.4.8	Oral anticoagulant therapy, ICPC code B34	22
4.4.9	Haemochromatosis, ICPC code A79.....	22
4.4.10	Anaemia, ICPC code B80	23
4.4.11	Increased bleeding tendency, ICPC code B83.....	25
4.4.12	HIV infection, ICPC code B90.....	25
4.4.13	Diarrhoea, ICPC code D11	25
4.4.14	Neonatal jaundice, ICPC code D13	25
4.4.15	Aphtous ulcer, ICPC code D83	25
4.4.16	Hiccups, ICPC code D29.....	25
4.4.17	Liver disease, ICPC code D97.....	26

4.4.18 Gastro-oesophageal disease, dyspepsia, ICPC code 84	26
4.4.19 Diverticular disease and diverticulitis, ICPC code D92	27
4.4.20 Irritable bowel syndrome, ICPC code D93	27
4.4.21 Coeliac disease, ICPC code D94	27
4.4.22 Cardiovascular risk calculation, ICPC code K22	27
4.4.23 Angina pectoris, ICPC code K74	28
4.4.24 Acute coronary syndrome, ICPC code K74-75	28
4.4.25 Heart failure, ICPC code K77	29
4.4.26 Atrial fibrillation, ICPC code K78	30
4.4.27 Hypertension, ICPC code K86	30
4.4.28 Transient ischemic attack, ICPC code K89	31
4.4.29 Pulmonary embolism, ICPC code K93	31
4.4.30 Deep venous thrombosis, ICPC code K94	31
4.4.31 Thrombophlebitis, ICPC code K94	32
4.4.32 Rheumatoid arthritis, ICPC code L88	32
4.4.33 Osteoporosis, ICPC code L95	34
4.4.34 Epilepsy, ICPC code N88	34
4.4.35 Insomnia, ICPC code P06	35
4.4.36 Alcohol problems, ICPC code P16-16	35
4.4.37 Dementia, ICPC code P70	35
4.4.38 Delirium, ICPC code	36
4.4.39 Anxiety disorder, ICPC code P74	36
4.4.40 Bipolar disorder, ICPC code P76	36
4.4.41 Depression, ICPC code P76	37
4.4.42 Eating disorders, ICPC code P86	37
4.4.43 Acute cough, ICPC code R05	37
4.4.44 Sore throat, ICPC code R21	37
4.4.45 Influenza, ICPC code R80	37
4.4.46 Acute lower respiratory tract infection, ICPC code R81	37
4.4.47 Chronic obstructive pulmonary disease, ICPC code R95	38
4.4.48 Asthma, ICPC code R96	38
4.4.49 Allergic rhinitis, ICPC code R98	38
4.4.50 Eczema, ICPC code S87	38
4.4.51 Acne, ICPC code S96	38
4.4.52 Venous ulcer, ICPC code S97	38
4.4.53 Urticaria, ICPC code S98	39
4.4.54 Obesity, ICPC code T82	39
4.4.55 Thyroid disorders, ICPC code T85-T86	39
4.4.56 Diabetes mellitus, ICPC code T89-T90	40
4.4.57 Gout, ICPC code T92	41

4.4.58	Dysuria in older men, ICPC code U01-U02.....	41
4.4.59	Renal failure, ICPC code U28.....	42
4.4.60	Urinary tract infections, ICPC code U71.....	42
4.4.61	Hyperemesis gravidarum, ICPC code W05.....	42
4.4.62	Subfertility, ICPC code W15.....	42
4.4.63	Pregnancy, ICPC code W78.....	42
4.4.64	Amenorrhoea, ICPC code X05.....	43
4.4.65	Excessive menstruation, ICPC code X06.....	44
4.4.66	Menopause, ICPC code X11.....	44
4.4.67	Postmenopausal bleeding, ICPC code X12.....	44
4.4.68	Syphilis, ICPC code X70-Y70.....	44
4.4.69	Gonorrhoea, ICPC code X71-Y71.....	44
4.4.70	Trichomoniasis, ICPC code X73.....	44
4.4.71	Bacterial vaginosis, ICPC code X84.....	45
4.4.72	Genital herpes, ICPC code X90-Y72.....	45
4.4.73	Chlamydia, ICPC code X92.....	45
4.4.74	Pelvic inflammatory disease, ICPC code X74.....	45
4.4.75	Prostate cancer, ICPC code Y77.....	45
4.4.76	Benign prostate hypertrophy, ICPC code Y85.....	45
4.5	DISCUSSION.....	46
5	PROSPECTIVE STUDY IN GENERAL PRACTICE ON THE MOTIVATION OF LABORATORY TEST UTILISATION.....	47
5.1	INTRODUCTION.....	47
5.2	METHODOLOGY.....	47
5.2.1	Study population.....	47
5.2.2	Data collection.....	47
5.2.3	Analysis.....	48
5.3	RESULTS.....	48
5.3.1	Characteristics of Laboratories and GPs.....	48
5.3.2	Patient characteristics.....	49
5.3.3	Laboratory test orders.....	49
5.3.4	Individual tests.....	51
5.3.5	Laboratory test orders per clinical indication.....	56
5.3.6	Analysis of individual tests.....	73
5.4	DISCUSSION.....	76
6	INTERVENTIONS TO INFLUENCE LABORATORY TESTS ORDERING.....	78
6.1	INTRODUCTION.....	78
6.2	METHODOLOGY.....	78
6.3	RESULTS.....	79

6.3.1	Systematic review.....	79
6.3.2	Update of the systematic review	79
6.4	DISCUSSION	81
6.5	CONCLUSIONS.....	83
7	GENERAL DISCUSSION	84
8	POLICY RECOMMENDATIONS.....	86
9	REFERENCES	87
10	APPENDIX.....	90

I 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 underused¹.

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 requests². Unexplained complaints and patients' expectations have also been shown to increase the likelihood of laboratory tests being ordered³.

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 purposes⁴. 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 ordering⁵.

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, were 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 erythrocytes
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
Hormonology	C-peptide
	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 (\square 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 (Waalser 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 prostaatankerscreening” (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.

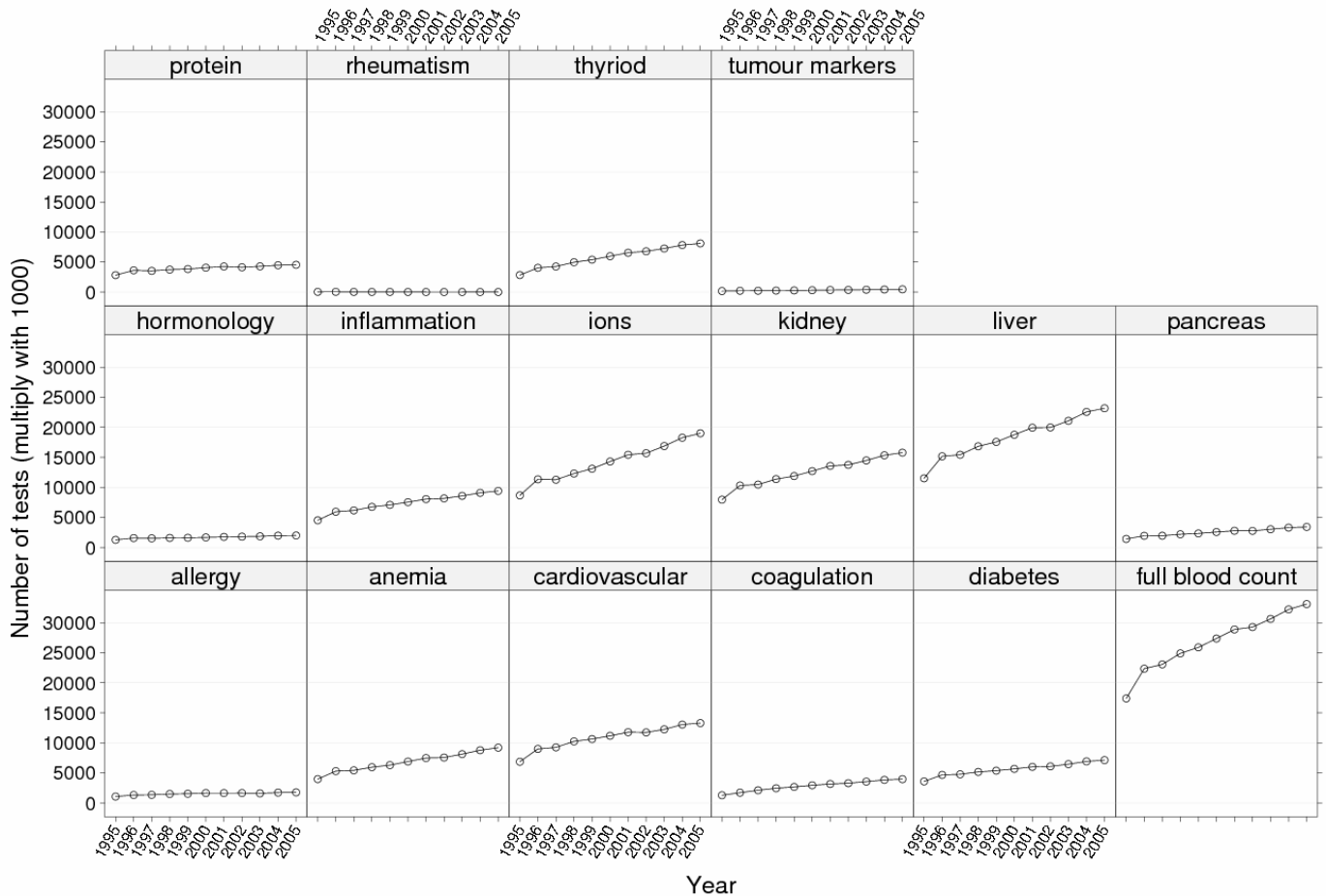


Figure 2.1 Number of tests (thousands) per cluster in function of year.

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).

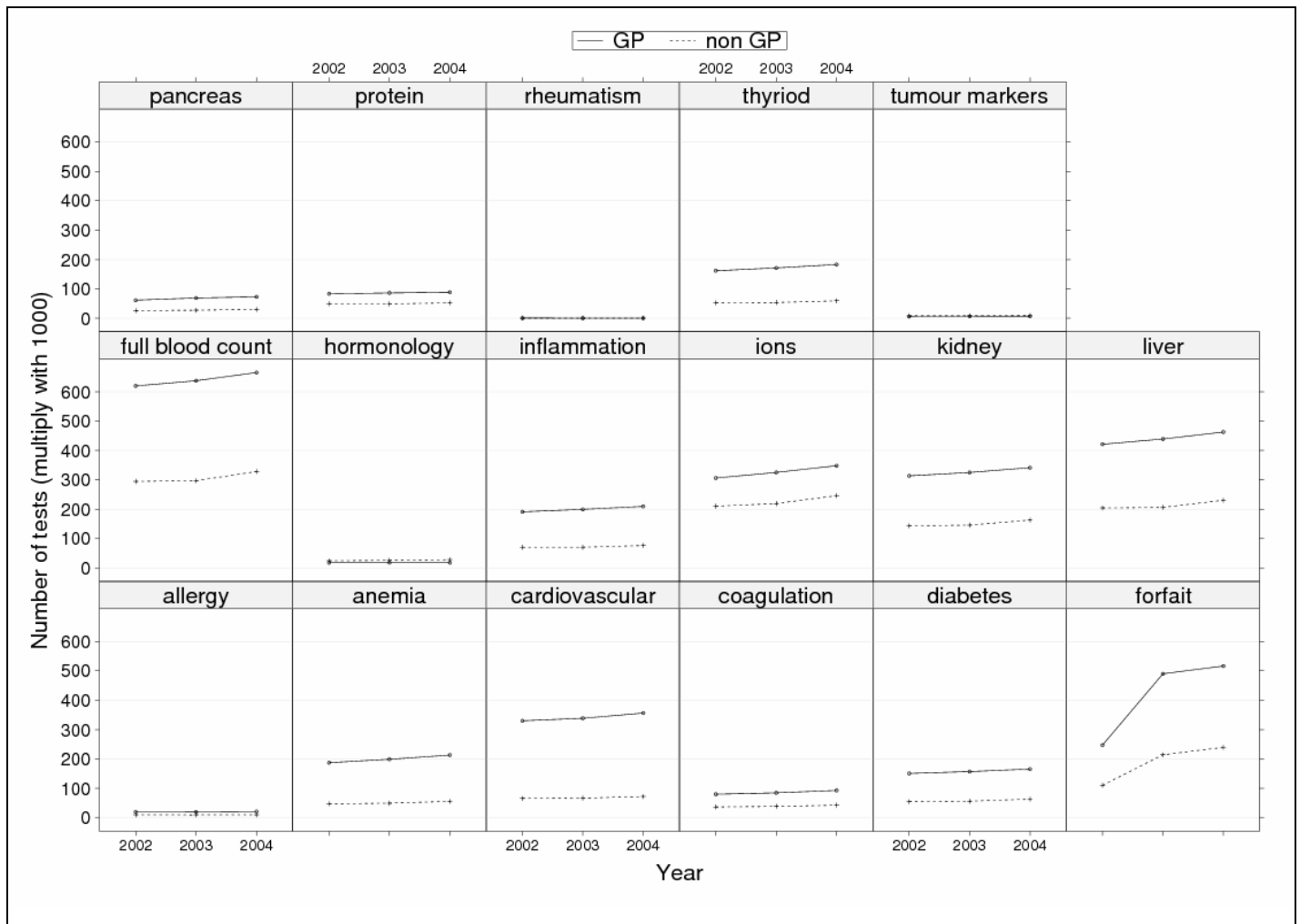
Detail of use of the selected laboratory tests on the level of the nomenclature numbers within each subcluster can be found in the appendix to this chapter.

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.

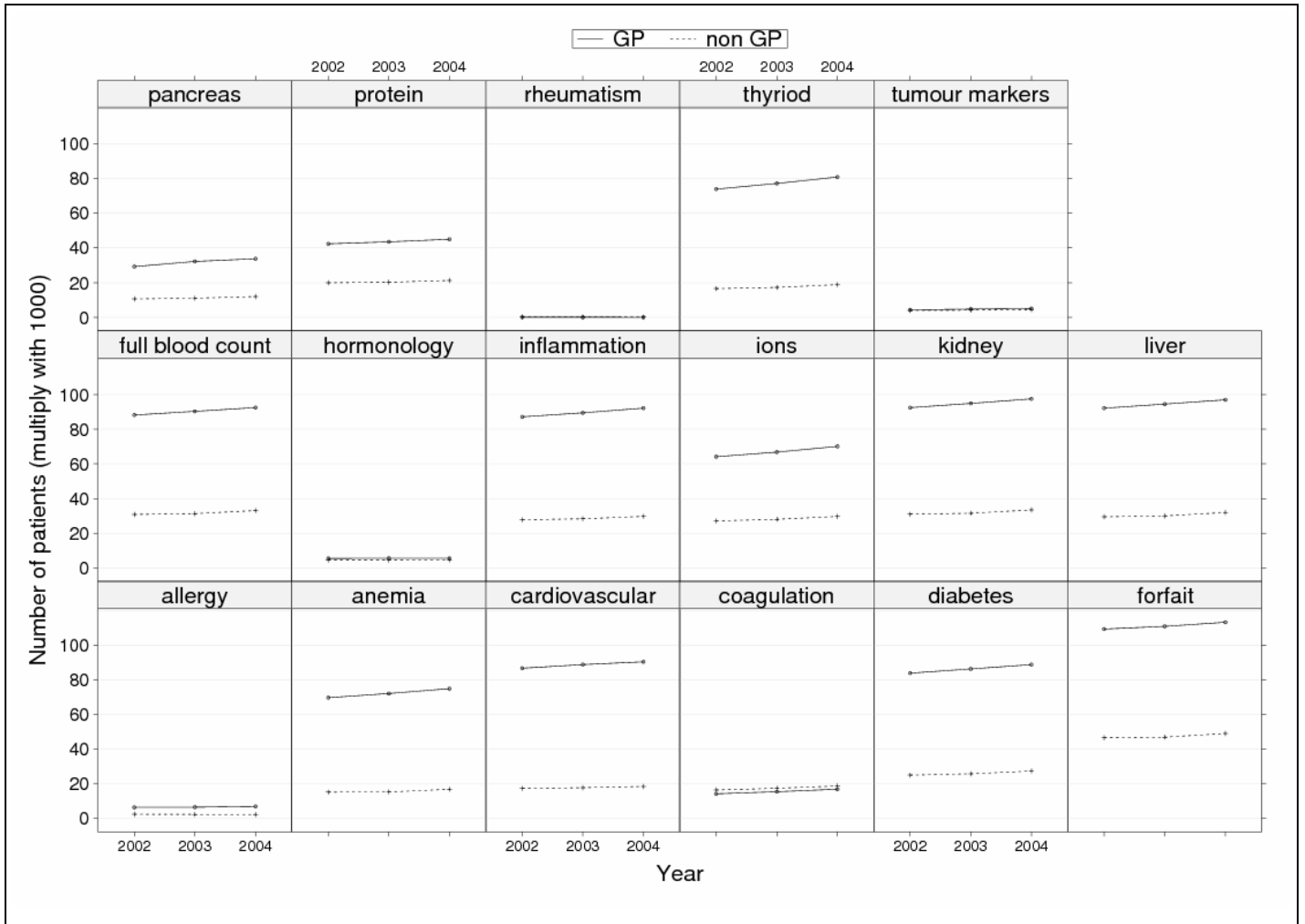
The effect of test order type in the hormonology tests was most pronounced in progesterone, LH, and estradiol (see figure 2.2sub2 in appendix on p. 115). The other subclusters showed a more moderate difference in ordering behaviour between GPs and other specialists.

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.

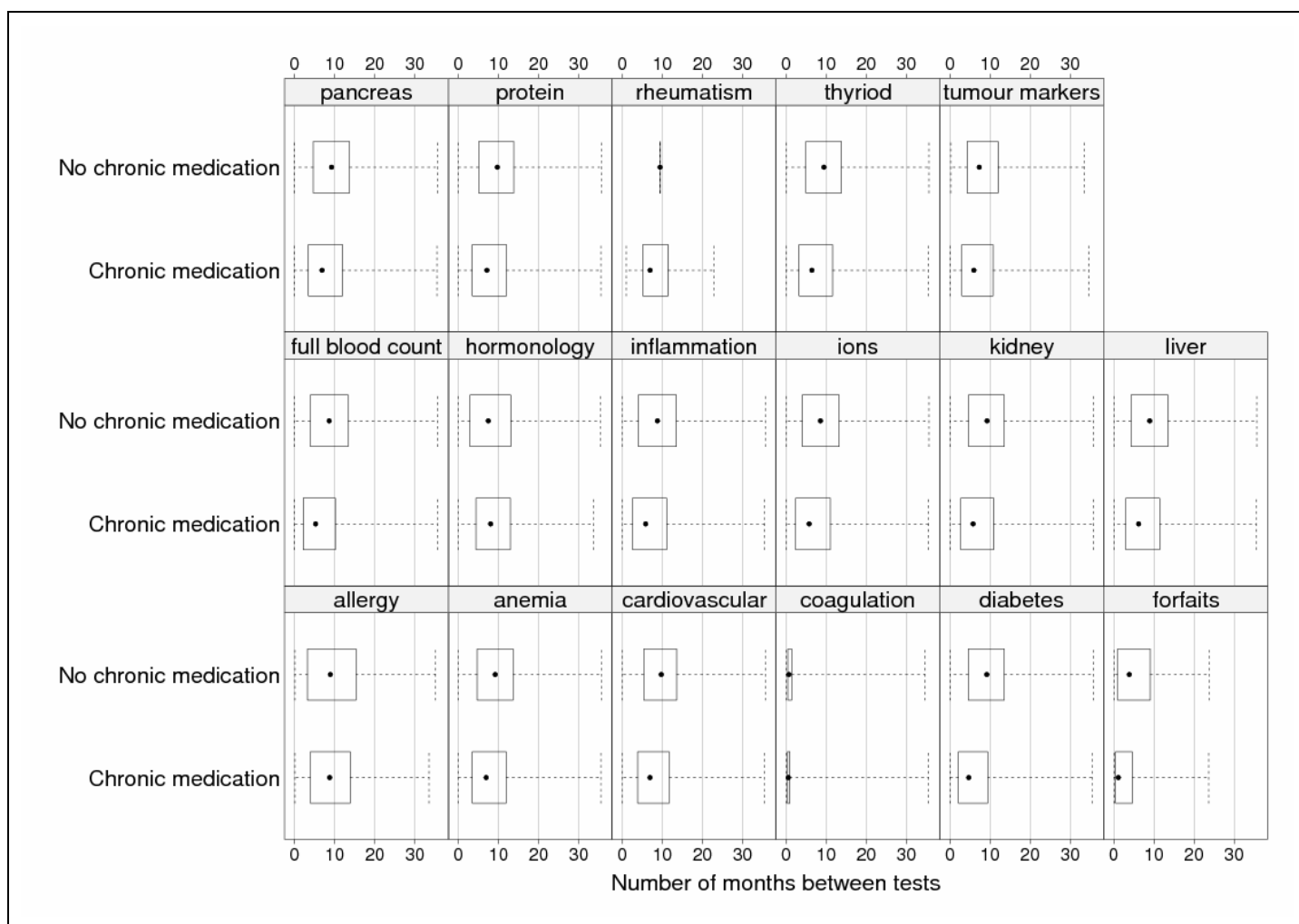
Figure 2.3 Number of patients (in thousands) in the IMA sample per year in function of cluster and specialism.



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 2.4subI 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

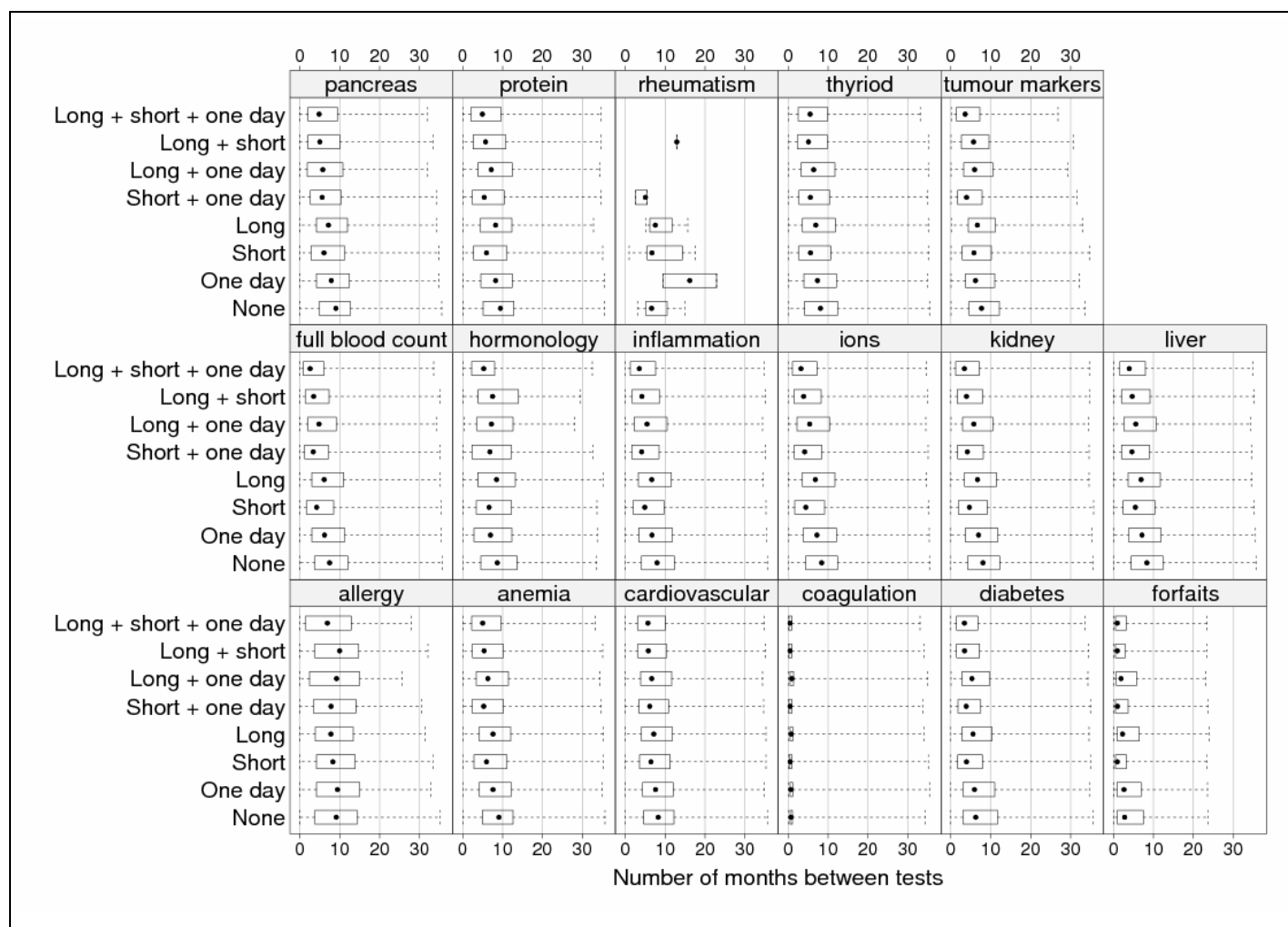
There was a general tendency for smaller intervals of time between consecutive tests for patients that had longer types of hospitalisation in the period 2002-2004 (see table 2.2 and figure 2.5).

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.



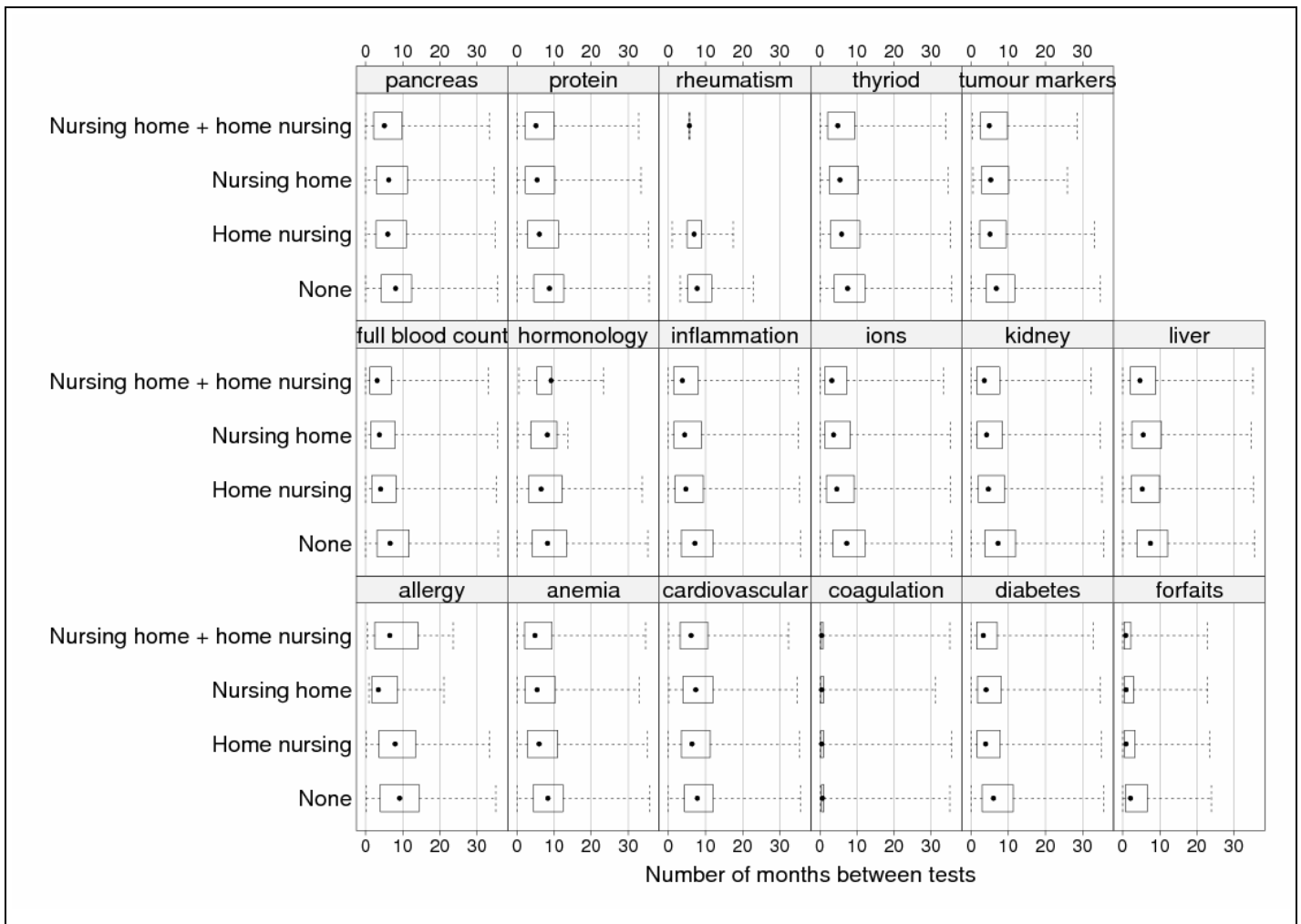
2.3.2.4 Patient characteristics: care status

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 patient¹⁰. The probability of false positive results increases, leading to unnecessary concern and additional testing or initiating inappropriate treatment¹¹.

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 therapy¹².

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 review¹³⁻²¹. 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 centre¹³. 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 abnormal¹⁸. 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 practice²⁰. 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 determined¹⁹.

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-effective²⁴. 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 management¹². 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.

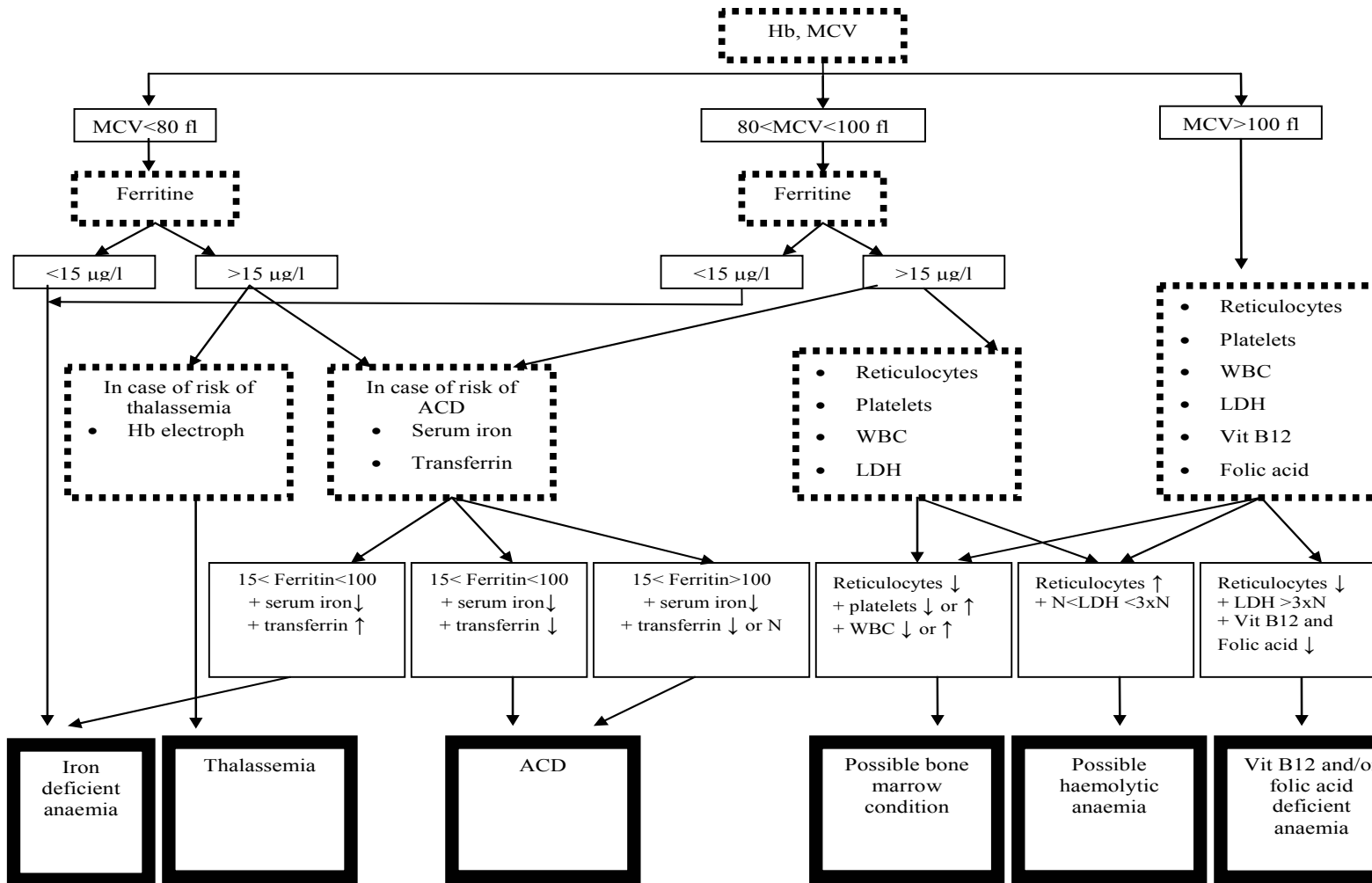
The algorithm below summarises the recommendations.

Abbreviations used:

ACD = anaemia by chronic condition

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

- Hb



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 Aphthous 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 I.

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 PI6-I6

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 NZGG:

- 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 ulcer, ICPC code S97

One guideline was available, by Prodigy.

The following lab tests are recommended in patients diagnosed with a venous ulcer 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	√			

WVVH assigns level I to these recommendations, NZZG grade D.

4.4.56.3 Follow-up of glycaemia control

All five guidelines recommend the following tests to monitor glycaemic control in both type I 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	WVWH	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 as 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. Papanicolaou 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.

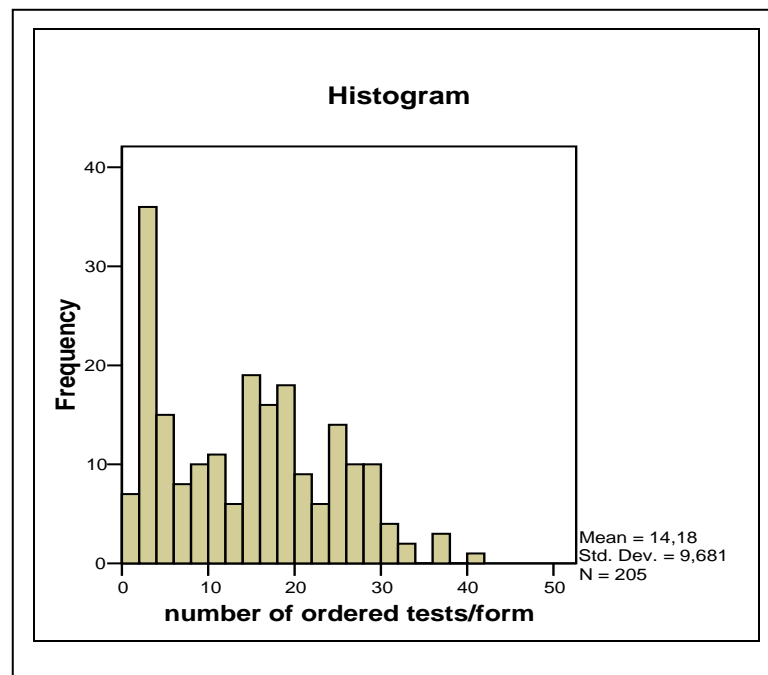
On average an order for diabetes contained 13.5 tests (SD 9.2) and cost 39.5 € (SD 13.6 €). The personal contribution of the patient was on average 7.1 € (SD 5.4 €).

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 (0.41)
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, K 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 main 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. Jamtvedt²⁵ 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 guidelines²⁶. 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 study¹⁴ 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 review²⁷ 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 Kingdom¹⁹, 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 I 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 Baker²⁹ 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 Ib).

The cluster randomised trial of Flottorp³⁰ 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 evidence 1b).

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 [\pm 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 reintroduced²⁰. The periods differ significantly, but this is totally due to the intervention period ($p<0.001$) (level of evidence 2a).

Smithuis²⁸ 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 Gend²¹ 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 quality³¹, 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 Zealand³² 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 study³³, 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 used³⁴.

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. Verstappen¹⁰ 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: their 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 GPs³⁵ 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 antibiotics³⁶. 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 some³⁷, but this has not been proven as yet²⁵. 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 limited²⁵. The notion of interventions targeted at many behavioural factors as described by Solomon et al.²⁷ is similar to these multifaceted interventions³⁷. Several important and rigorous 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 tests 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.

9 REFERENCES

1. Lodewyckx KP, Gert; Spitz, Bernard; Blot, Stijn; Temmerman, Marleen; Zhang, Weihong; Alexander, Sophie; Mambourg, Françoise; Ramaekers, Dirk. Nationale richtlijn prenatale zorg. Een basis voor een klinisch pad voor de opvolging van zwangerschappen. In: Gezondheidszorg FKvd, editor, 2004.
2. Verstappen WH, ter Riet G, Dubois WI, Winkens R, Grol RP, van der Weijden T. Variation in test ordering behaviour of GPs: professional or context-related factors? *Fam Pract* 2004;21(4):387-95.
3. van der Weijden T, van Velsen M, Dinant GJ, van Hasselt CM, Grol R. Unexplained complaints in general practice: prevalence, patients' expectations, and professionals' test-ordering behavior. *Med Decis Making* 2003;23(3):226-31.
4. Prochazka AV, Lundahl K, Pearson W, Oboler SK, Anderson RJ. Support of evidence-based guidelines for the annual physical examination: a survey of primary care providers. *Arch Intern Med* 2005;165(12):1347-52.
5. van der Weijden T, van Bokhoven MA, Dinant G-J, van Hasselt CM, Grol RPTM. Understanding laboratory testing in diagnostic uncertainty: a qualitative study in general practice. *Br J Gen Pract* 2002;52(485):974-80.
6. Sectoraal Comité van de Sociale Zekerheid. Beraadslaging nr. 05/033 van 19 juli 2005 met betrekking tot het project 2004-21 impact van het innen van supplementen op de toegankelijkheid van de gezondheidszorg, 2005.
7. Degauquier K, Diels J, Di Zinno T, Guillaume J, Mertens R. *Preoperatieve onderzoeken 2003. Feedback kwaliteitspromotie*. Brussel: Inter mutualistisch Agentschap, 2005.
8. Institute S. SAS 9.1.3. Cary, NC, 2006.
9. Team RDC. *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing, 2007.
10. Verstappen WHJM, Van Der Weijden T, Sijbrandij J, Smeele I, Hermsen J, Grimshaw J, et al. Effect of a Practice-Based Strategy on Test Ordering Performance of Primary Care Physicians: A Randomized Trial. *Journal of the American Medical Association* 2003;289(18):2407-2412.
11. Knottnerus JA, van Weel C, Muris JW. Evaluation of diagnostic procedures. *Bmj* 2002;324(7335):477-80.
12. van Walraven C, Naylor CD. Do we know what inappropriate laboratory utilization is? A systematic review of laboratory clinical audits. *Jama* 1998;280(6):550-8.
13. Carraro P, Simioni P. Appropriateness of choice and interpretation of tests for thrombophilic defects: a practical experience. *Clin Chim Acta* 2003;333(2):191-3.
14. Larsson A, Biom S, Wernroth ML, Hulten G, Tryding N. Effects of an education programme to change clinical laboratory testing habits in primary care. *Scand J Prim Health Care* 1999;17(4):238-43.
15. Malcolm L, Wright L, Seers M, Davies L, Guthrie J. Laboratory expenditure in Pegasus Medical Group: a comparison of high and low users of laboratory tests with academics. *N Z Med J* 2000;113(1105):79-81.
16. Winkens RA, Pop P, Grol RP, Bugter-Maessen AM, Kester AD, Beusmans GH, et al. Effects of routine individual feedback over nine years on general practitioners' requests for tests. *BMJ* 1996;312(7029):490.
17. van Wijk MA, van der Lei J, Mosseveld M, Bohnen AM, van Bommel JH. Assessment of decision support for blood test ordering in primary care. a randomized trial. *Ann Intern Med* 2001;134(4):274-81.
18. Schectman JM, Elinsky EG, Pawlson LG. Self-reported versus actual test ordering behavior among primary care clinicians. *QRB Qual Rev Bull* 1992;18(2):60-2.

19. Bailey J, Jennings A, Parapia L. Change of pathology request forms can reduce unwanted requests and tests. *J Clin Pathol* 2005;58(8):853-5.
20. Zaat JO, van Eijk JT, Bonte HA. Laboratory test form design influences test ordering by general practitioners in The Netherlands. *Med Care* 1992;30(3):189-98.
21. van Gend JM, van Pelt J, Cleef TH, Mangnus TM, Muris JW. [Quality improvement project 'laboratory diagnosis by family physicians' leads to considerable decrease in number of laboratory tests]. *Ned Tijdschr Geneesk* 1996;140(9):495-500.
22. Nuutila P, Irjala K, Viikari J, Prinssi VP, Kaihola HL. Comparative evaluation of serum thyroxine, free thyroxine and thyrotropin determinations in screening of thyroid function. *Ann Clin Res* 1988;20(3):158-63.
23. Ericsson UB, Fernlund P, Thorell JI. Evaluation of the usefulness of a sensitive immunoradiometric assay for thyroid stimulating hormone as a first-line thyroid function test in an unselected patient population. *Scand J Clin Lab Invest* 1987;47(3):215-21.
24. Schectman JM, Pawlson LG. The cost-effectiveness of three thyroid function testing strategies for suspicion of hypothyroidism in a primary care-setting. *J Gen Intern Med* 1990;5(1):9-15.
25. Jamtvedt G, Young JM, Kristoffersen DT, Thomson O'Brien MA, Oxman AD. Audit and feedback: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev* 2003(3):CD000259.
26. Grimshaw JM, Shirran L, Thomas R, Mowatt G, Fraser C, Bero L, et al. Changing provider behavior: an overview of systematic reviews of interventions. *Med Care* 2001;39(8 Suppl 2):II2-45.
27. Solomon DH, Hashimoto H, Daltroy L, Liang MH. Techniques to improve physicians' use of diagnostic tests: a new conceptual framework. *JAMA* 1998;280(23):2020-7.
28. Smithuis. Beperking van het laboratoriumonderzoek door een probleemgeoriënteerd aanvraagformulier. *Huisarts en Wetenschap* 1994;37:464-466.
29. Baker R, Falconer Smith J, Lambert PC. Randomised controlled trial of the effectiveness of feedback in improving test ordering in general practice. *Scand J Prim Health Care* 2003;21(4):219-23.
30. Flottorp S, Havelsrud K, Oxman AD. Process evaluation of a cluster randomized trial of tailored interventions to implement guidelines in primary care - Why is it so hard to change practice? *Family Practice* 2003;20(3):333-339.
31. van Walraven C, Goel V, Chan B. Effect of population-based interventions on laboratory utilization: a time-series analysis. *JAMA* 1998;280(23):2028-33.
32. Kerr D, Malcolm L, Schousboe J, Pimm F. Successful implementation of laboratory budget holding by Pegasus Medical Group. *New Zealand Medical Journal* 1996;109(1029):334-7.
33. Thomas RE, Croal BL, Ramsay C, Eccles M, Grimshaw J. Effect of enhanced feedback and brief educational reminder messages on laboratory test requesting in primary care: a cluster randomised trial. *Lancet* 2006;367(9527):1990-6.
34. Knottnerus JA. Improving test ordering and diagnostic cost effectiveness in clinical practice-bridging the gap between clinical research and routine health care. In: Books B, editor. *The evidence base of clinical diagnosis*. London: BMJ Publishing Group, 2002:197-209.
35. Winkens RA, Grol RP, Beusmans GH, Kester AD, Knottnerus JA, Pop P. Does a reduction in general practitioners' use of diagnostic tests lead to more hospital referrals? *Br J Gen Pract* 1995;45(395):289-92.
36. Van Linden A HI, Mambourg F, Leys M, De Prins L, Dieleman P, Mensaert A, Vanhalewyn M., , 2005.. BA, Kenniscentrum F. Feedback: évaluation de l' impact et

des barrières à l'implémentation. Bruxelles: Centre Fédéral d' Expertise des Soins de Santé (KCE).

37. Grol R WM. *Implementatie. Effectieve verandering in de patiëntzorg.*, 2001.
38. Buntinx F, Knockaert D, Bruyninckx R, de Blaeij N, Aerts M, Knottnerus JA, et al. Chest pain in general practice or in the hospital emergency department: is it the same? *Fam Pract* 2001;18(6):586-9.
39. Knottnerus JA. The effects of disease verification and referral on the relationship between symptoms and diseases. *Med Decis Making* 1987;7(3):139-48.
40. Knottnerus JA, Leffers P. The influence of referral patterns on the characteristics of diagnostic tests. *J Clin Epidemiol* 1992;45(10):1143-54.
41. Flottorp S, Oxman AD, Havelsrud K, Treweek S, Herrin J. Cluster randomised controlled trial of tailored interventions to improve the management of urinary tract infections in women and sore throat. *BMJ* 2002;325(7360):367.

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	Nomenclature	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 erythrocytes	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	Nomenclature	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) (Diagnoseregul 54) Klasse 14					14787
	Total cholesterol	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	Nomenclature	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	Nomenclature	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), ⁶ afgeleid van de analyse van een differentieel volumetrisch his		47	66	26	28
		123196	Leucocytenformule (ten minste vijf populaties), vastgesteld met cellenteller en ⁷ gebaseerd op criteria die niet alleen de celgrootte omv		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), ¹¹ afgeleid van de analyse van een differentieel volumetrisch histogram, verkregen	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
	hemoglobine	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 trombocyten (Maximum 1) Klasse 2	3149	5196	3542	2210	2153
		127116	Tellen van de trombocyten (Maximum 1) Klasse 2	3146797	4095000	4241348	4617453	4842635

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

Cluster	Subcluster	Nomenclature	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	Nomenclature	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	Nomenclature	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 hepatis	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	Nomenclature	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	Waalser Rose	124530	Test van Waalser Rose op plaatje (Maximum 1) Klasse 3	2102	2420	2166	2202	2074
		128531	Test van Waalser 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-thyroid microsome of anti-thyroperoxydase 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	Nomenclature	Label (dutch)	1995	1996	1997	1998	1999
	T3 total	435013	Doseren van totale triiodothyronine (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 I/Bloed : Dosereren van C E A (Maximum I	66134	70823	51491	47014	33573
		548332	Therapeutische Monitoring I/Bloed : Dosereren van C E A met niet isotopenmethode (Maximum I) (Cumulregel 201, 317) (Diagnoseregel 46) Klasse	28048	49030	67382	81271	105044
	CA 15.3	436170	Therapeutische Monitoring I/Bloed : Dosereren van CA 15 3 (Maximum	42905	50524	45051	46667	37633
		548310	Therapeutische Monitoring I/Bloed : Dosereren van CA 15 3 met niet isotopenmethode (Maximum I) (Cumulregel 201, 315) (Diagnoseregel 46) Klass	14996	24469	33637	45490	70313
	CA 19-10	548354	Therapeutische Monitoring I/Bloed : Dosereren van carbohydrate antigen 19-9 (CA 19-9) (Maximum I)(Cumulregel 201)(Diagnoseregel 46) Klasse 20	3022	5660	7898	10771	14415
	CA 19-9	436214	Therapeutische Monitoring I/Bloed : Dosereren 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	Nomenclature	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
anemia	ferritin	556253	Doseren van IgE totaal (Maximum 1)(Cumulregel 46) Klasse 13	272565	298132	343075	368604	400519	408245
		433090	Doseren van ferritine (Maximum 1) (Cumulregel 305) Klass	362002	204345	149767	135327	87804	77030
	Folic acid	541472	Doseren van ferritine met niet isotopenmethode (Maximum 1) (Cumulregel 305) Klasse 13	1920518	2300939	2416480	2636749	2921687	3095087
		433053	Doseren van foliumzuur in het serum (Maximum 1) (Cumulregel 303) Klasse 13	19016	17407	17533	10893	8747	6694
	Folic acid erythrocytes	541435	Doseren van foliumzuur in het serum met niet isotopenmethode (Maximum 1) (Cumulregel 303) Klasse 13	29173	37190	47350	69857	73994	68963
		433075	Doseren van foliumzuur in de erythrocyten (Maximum 1) (C	58600	55907	47740	39971	32862	16916
	Iron	541450	Doseren van foliumzuur in de erythrocyten met niet isotopenmethode (Maximum 1) (Cumulregel 304) Klasse 14	65564	82722	95087	122552	144328	173020
		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	Nomenclature	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	Nomenclature	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	Nomenclature	Label (dutch)	2000	2001	2002	2003	2004	2005
		123174	Vereenvoudigde leucocytenformule (lymfocyten, monocyt 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, monocyt 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	Nomenclature	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	Nomenclature	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	Nomenclature	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	Nomenclature	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	Nomenclature	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	Waalser Rose	124530	Test van Waalser Rose op plaatje (Maximum 1) Klasse 3	1560	238	211	169	134	104
		128531	Test van Waalser 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-thyriod microsomien of anti-thyrioperoxidase 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	Nomenclature	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 triiodothyronine (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	Nomenclature	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 I/Bloed : Doseren van C E A (Maximum 1	25275	19991	13159	9569	7817	5535
		548332	Therapeutische Monitoring I/Bloed : Doseren van C E A met niet isotopenmethode (Maximum 1) (Cumulregel 201, 317) (Diagnoseregul 46) Klasse	130238	146509	159777	179619	194745	212894
	CA 15.3	436170	Therapeutische Monitoring I/Bloed : Doseren van CA 15 3 (Maximum	35216	33223	30607	21657	15750	12003
		548310	Therapeutische Monitoring I/Bloed : Doseren van CA 15 3 met niet isotopenmethode (Maximum 1) (Cumulregel 201, 315) (Diagnoseregul 46) Klass	82963	105286	118008	141594	163434	176097
	CA 19-10	548354	Therapeutische Monitoring I/Bloed : Doseren van carbohydrate antigen 19-9 (CA 19-9) (Maximum 1)(Cumulregel 201)(Diagnoseregul 46) Klasse 20	18478	22609	26091	31333	36710	41700
	CA 19-9	436214	Therapeutische Monitoring I/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).

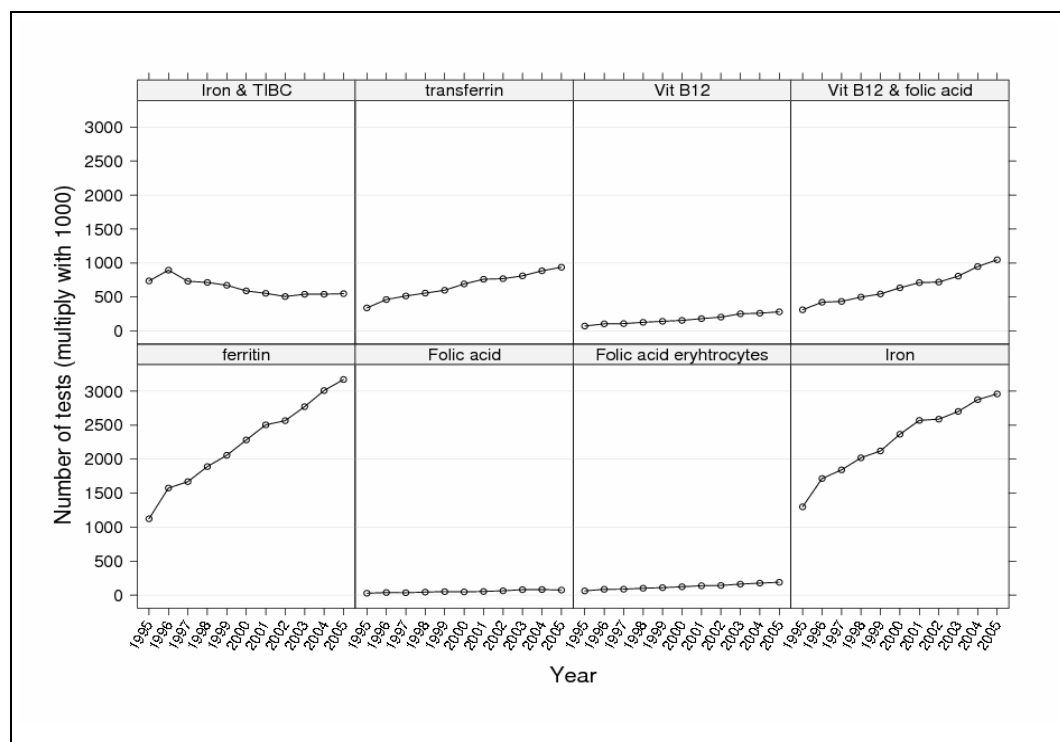


Figure 2.1sub2 Number of tests per subcluster for diabetes tests in function of year.

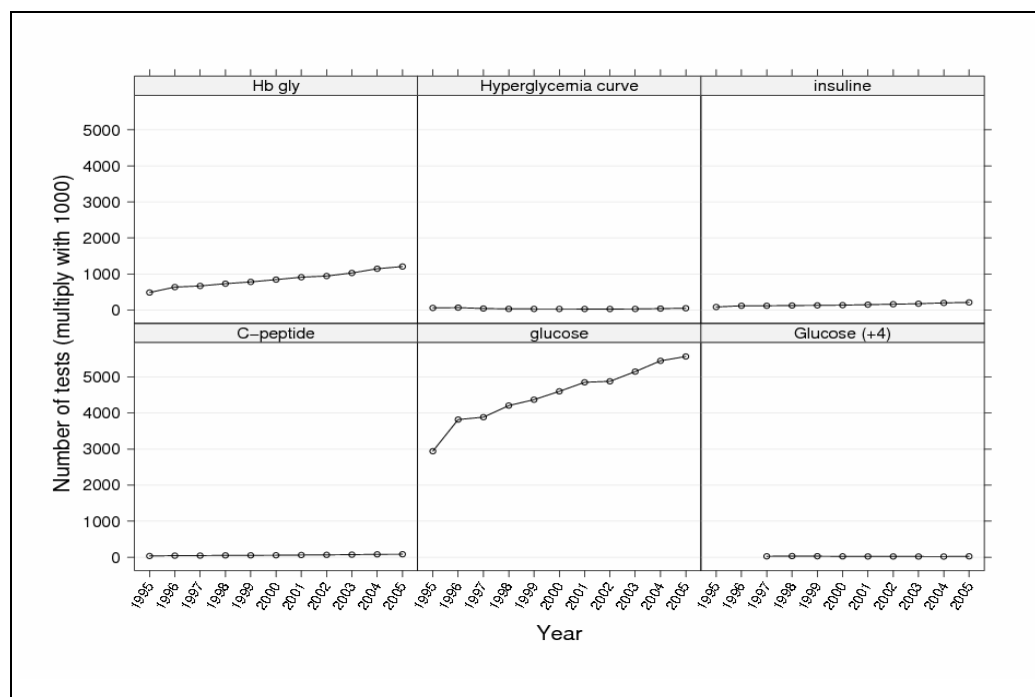


Figure 2.2sub1 Number of laboratory tests in the IMA sample per year in function of specialism and subclusters of tumour markers

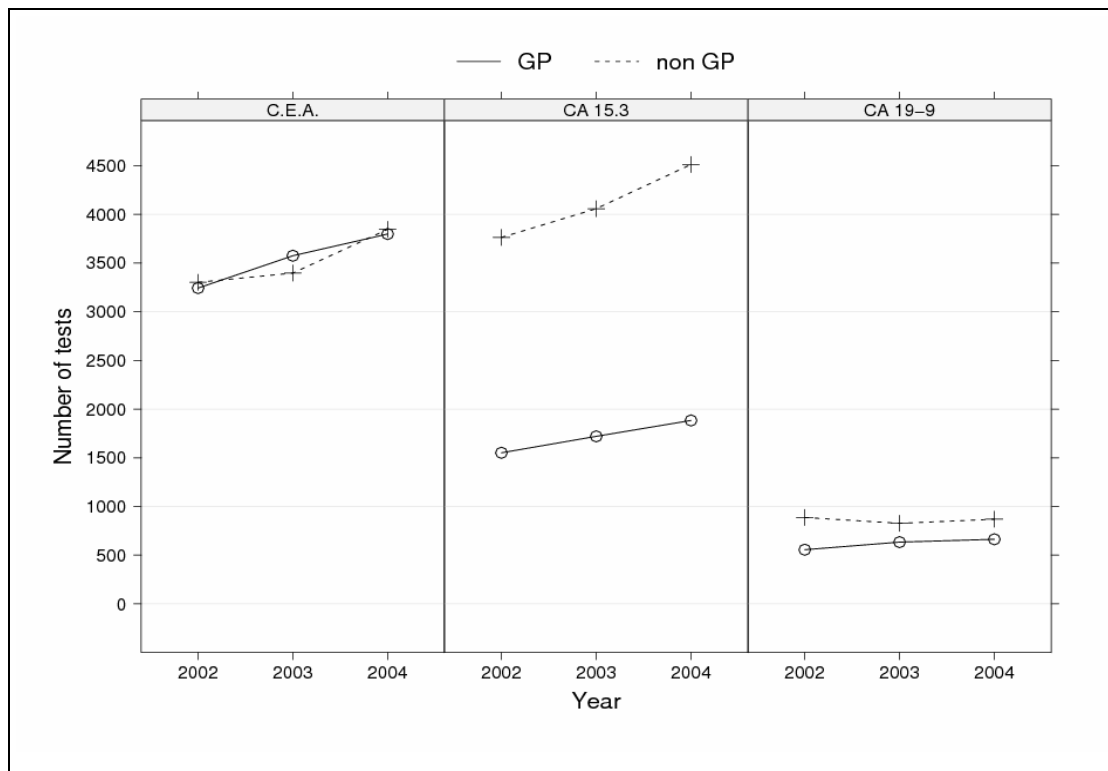


Figure 2.2sub2 Number of laboratory tests in the IMA sample per year in function of specialism and subclusters of hormonology

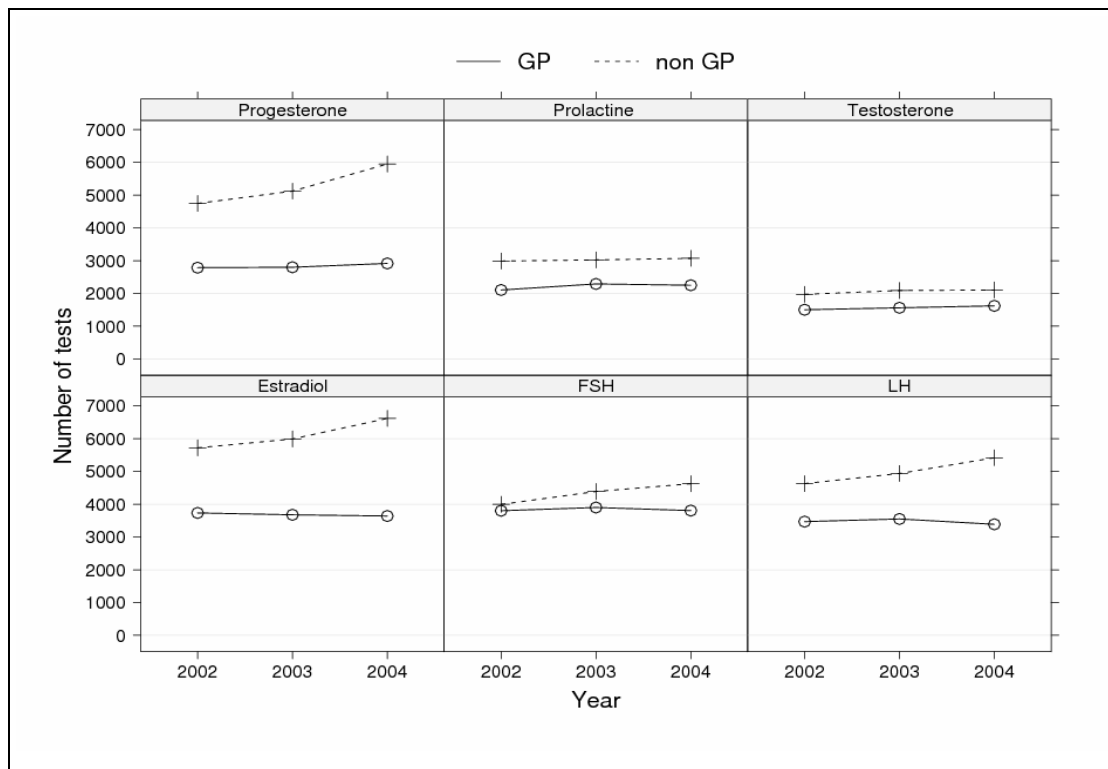


Figure 2.2sub3 Number of laboratory tests in the IMA sample per year in function of specialism and subclusters of coagulation

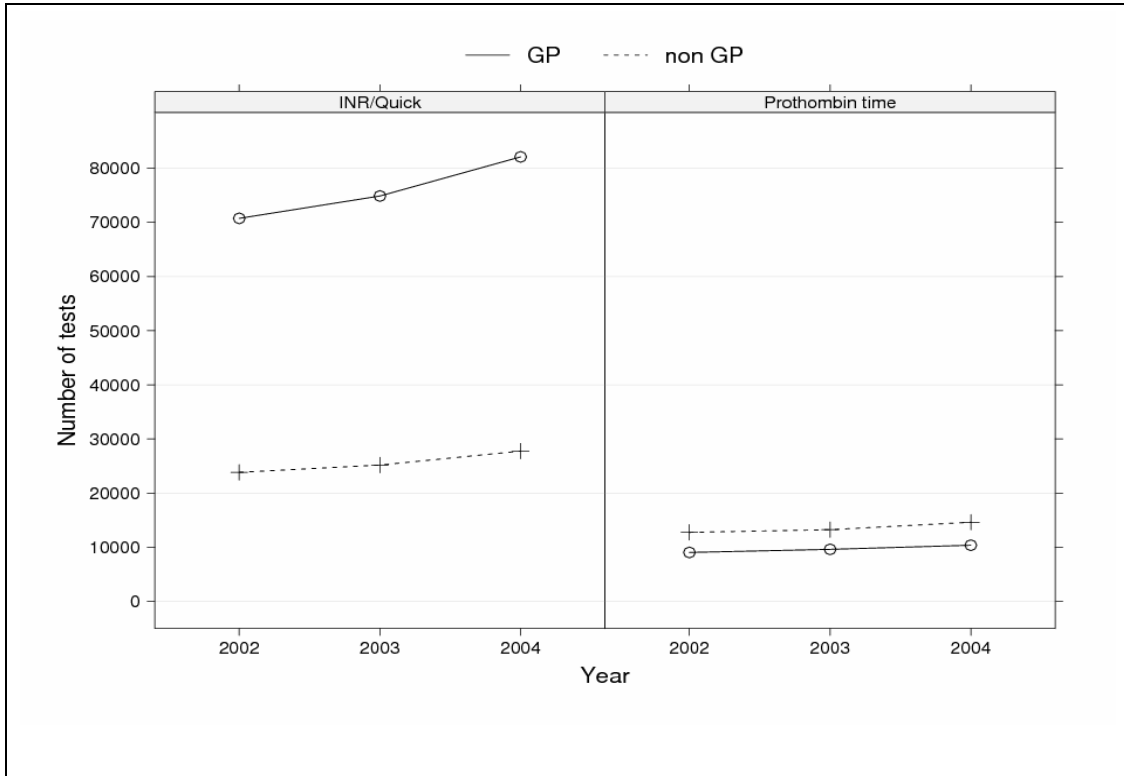


Figure 2.4sub1 Distribution of number of months between the order of the same laboratory test per patient in the period 2002 – 2004 ordered by GP's in function of laboratory test subcluster for the hormonology tests and chronic medication use (whiskers represent minimum and maximum values).

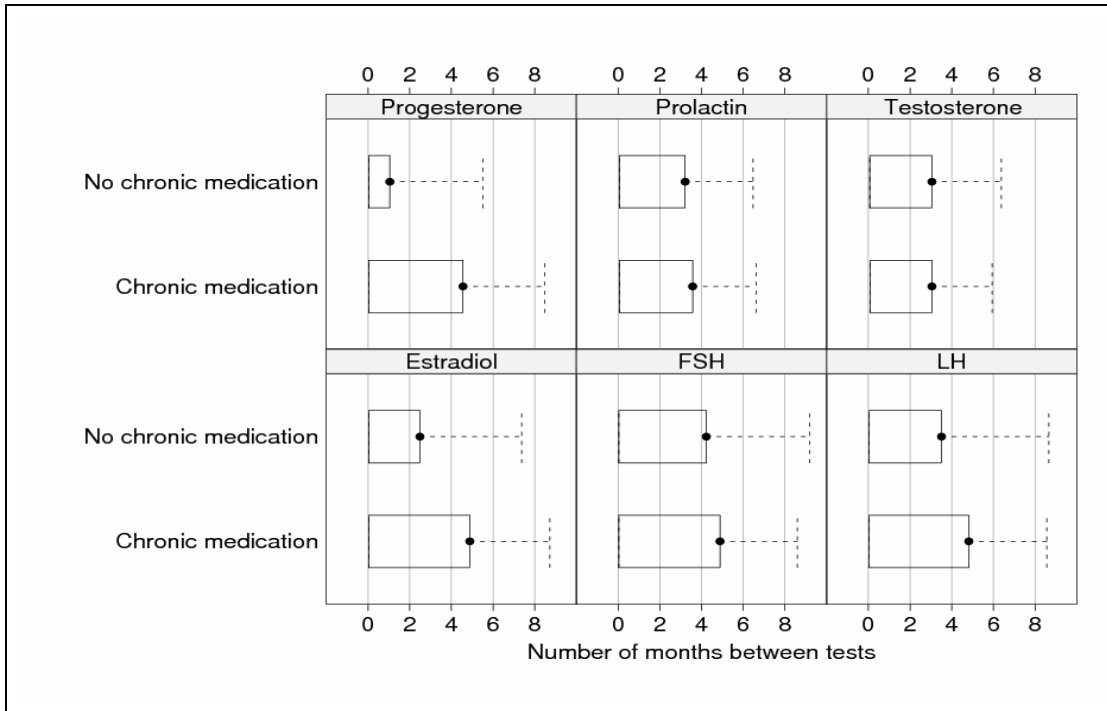
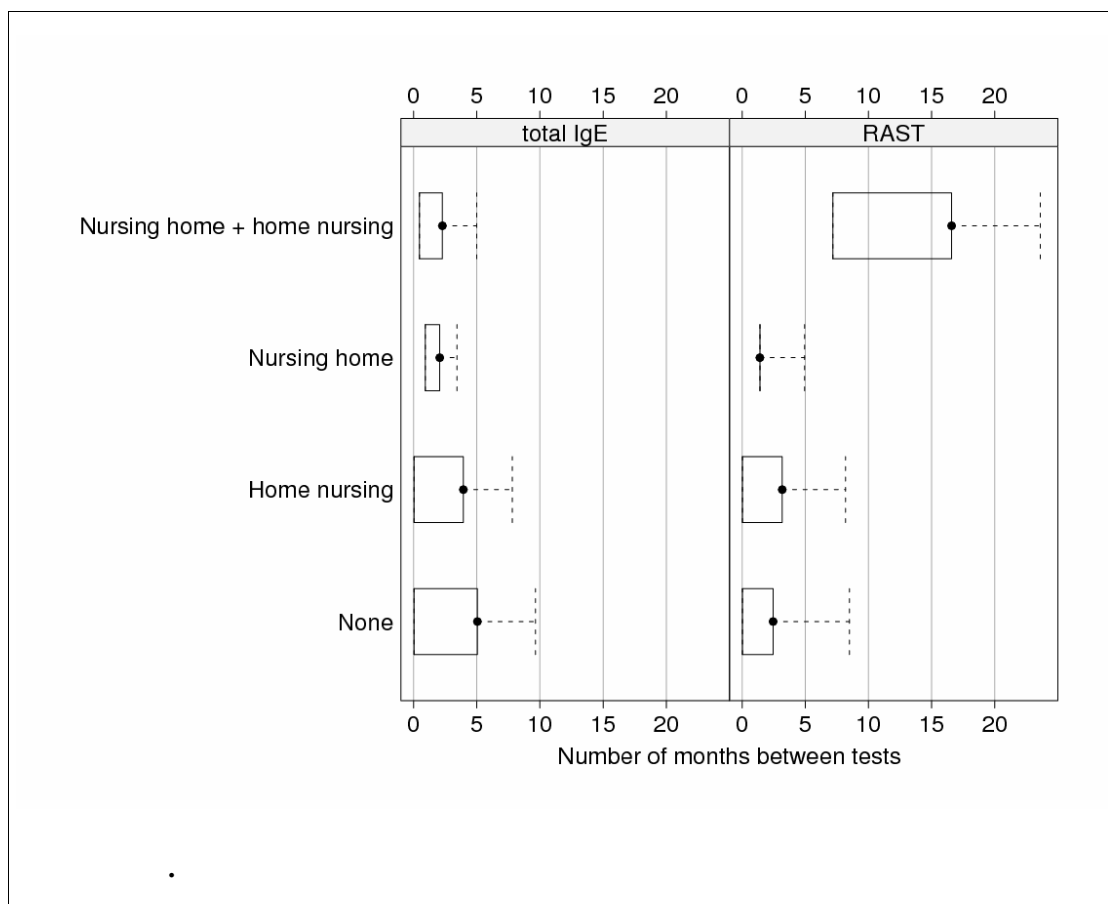


Figure 2.6subI Distribution of number of months between the order of the same laboratory test per patient in the period 2002 – 2004 ordered by GP's in function of subclusters for the allergy tests and care status (whiskers represent minimum and maximum values)



CHAPTER 3: APPROPRIATE USE OF LABORATORY TESTS IN GENERAL PRACTICE

Table 3.1 evidence tables of the included articles

Study ID	Carraro 2003	Larsson 1999	Malcolm 2000
Setting	Outpatient clinic of an academic medical center	General practices	General practice
Definition of (in)appropriate use	Based on guideline previously published; Antithrombin activity: pregnant women suspected of HELLP syndrome 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 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 Thrombophilia screening: Protein C Protein S Activated protein C resistance Homocysteinemia Genetic polymorphism of factor V Leiden Mutant prothrombin allele 20210A 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 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 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 tests advised against with recommended alternative (urea, thyroxine, free thyroxine, and triiodothyronine concentrations; Rose-Waaler and latex fixation tests) 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 Tests with a recommended alternative decreased by 85% 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 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 Calcium 0.38 LDH 0.21 RF 0.73 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	93.3			
differentiation				
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)
Musculoskeletal	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/ cardiovascular 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 additional)	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
Musculoskeletal		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)
Musculoskeletal		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/unspecified		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 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/unspecified		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	Ia	mixed strategy	Interventions based on multiple behavioural factors are more successful 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	Ib	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	Ib	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	Ib	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 inappropriate tests in arm A : significant reduction inappropriate test in arm B : not significant (arm A : tests for CV topics and abdominal complaints)	
Thomas Ruth 33 (UK)	cluster RCT	valid	Ib	quarterly feedback or educational messages as reminder or both	more than 20% reduction in the total test requested for interventions in combination 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 Van Wijk 2001 (Delft)	RCT	valid	Ib	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 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	Ib	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) 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) 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.

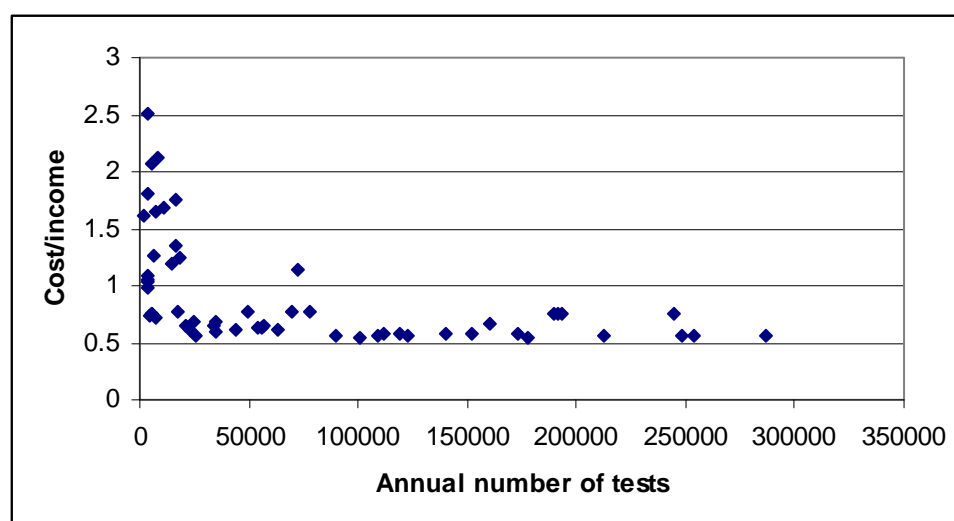
Table 4: Total annual number of tests, cost/test and real (RIZIV/IMAMI) income per test and theoretical income/test (including the forfaitary payment ventilated over the different tests) calculated on the basis of the data from a hospital-based medical laboratory.

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.

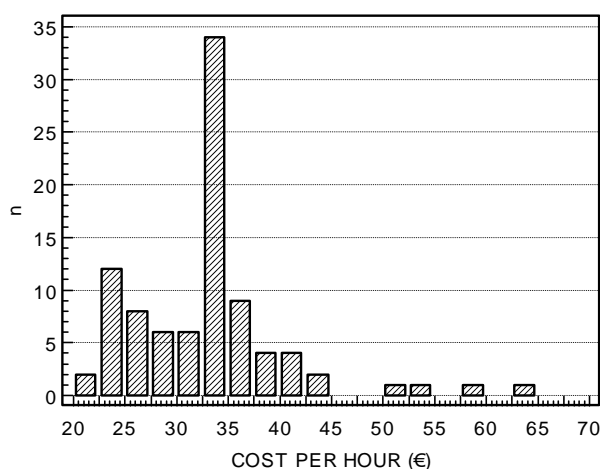
The extra time involved was calculated and multiplied with the average salary of a full-time laboratory technologist.

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/ebIm/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.

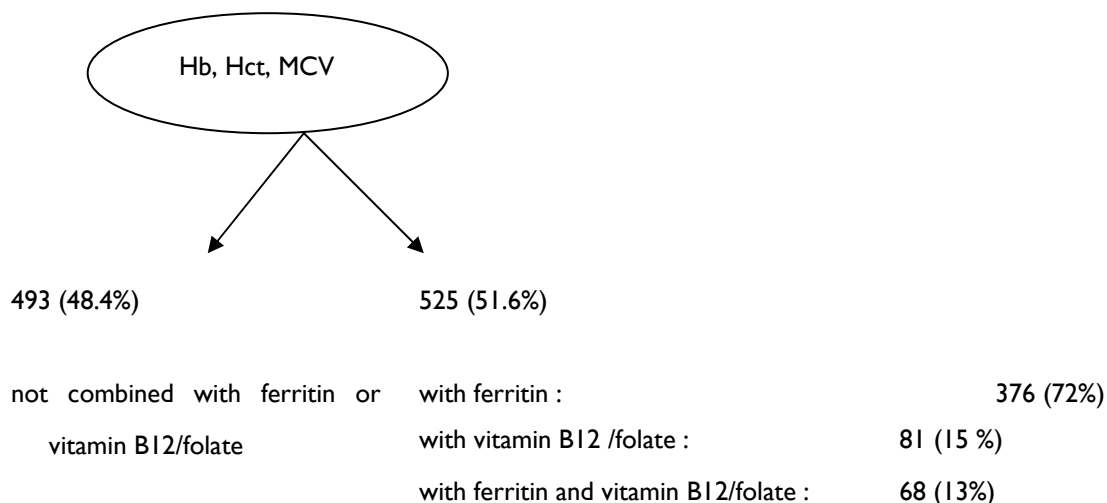


Figure 3: distribution of the combination of tests in the prospective study.

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 if 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	

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

²The 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
I 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	

¹Based 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.

This page is left intentionally blank.

KCE reports

1. Efficacité et rentabilité des thérapies de sevrage tabagique. D/2004/10.273/2.
2. Etude relative aux coûts potentiels liés à une éventuelle modification des règles du droit de la responsabilité médicale (Phase I). D/2004/10.273/4.
3. Utilisation des antibiotiques en milieu hospitalier dans le cas de la pyélonéphrite aiguë. D/2004/10.273/6.
4. Leucoréduction. Une mesure envisageable dans le cadre de la politique nationale de sécurité des transfusions sanguines. D/2004/10.273/8.
5. Evaluation des risques préopératoires. D/2004/10.273/10.
6. Validation du rapport de la Commission d'examen du sous financement des hôpitaux. D/2004/10.273/12.
7. Recommandation nationale relative aux soins prénatals: Une base pour un itinéraire clinique de suivi de grossesses. D/2004/10.273/14.
8. Systèmes de financement des médicaments hospitaliers: étude descriptive de certains pays européens et du Canada. D/2004/10.273/16.
9. Feedback: évaluation de l'impact et des barrières à l'implémentation – Rapport de recherche: partie I. D/2005/10.273/02.
10. Le coût des prothèses dentaires. D/2005/10.273/04.
11. Dépistage du cancer du sein. D/2005/10.273/06.
12. Etude d'une méthode de financement alternative pour le sang et les dérivés sanguins labiles dans les hôpitaux. D/2005/10.273/08.
13. Traitement endovasculaire de la sténose carotidienne. D/2005/10.273/10.
14. Variations des pratiques médicales hospitalières en cas d'infarctus aigu du myocarde en Belgique. D/2005/10.273/12
15. Evolution des dépenses de santé. D/2005/10.273/14.
16. Etude relative aux coûts potentiels liés à une éventuelle modification des règles du droit de la responsabilité médicale. Phase II : développement d'un modèle actuariel et premières estimations. D/2005/10.273/16.
17. Evaluation des montants de référence. D/2005/10.273/18.
18. Utilisation des itinéraires cliniques et guides de bonne pratique afin de déterminer de manière prospective les honoraires des médecins hospitaliers: plus facile à dire qu'à faire.. D/2005/10.273/20
19. Evaluation de l'impact d'une contribution personnelle forfaitaire sur le recours au service d'urgences. D/2005/10.273/22.
20. HTA Diagnostic Moléculaire en Belgique. D/2005/10.273/24, D/2005/10.273/26.
21. HTA Matériel de Stomie en Belgique. D/2005/10.273.28.
22. HTA Tomographie par Emission de Positrons en Belgique. D/2005/10.273/30.
23. HTA Le traitement électif endovasculaire de l'anévrisme de l'aorte abdominale (AAA). D/2005/10.273.33.
24. L'emploi des peptides natriurétiques dans l'approche diagnostique des patients présentant une suspicion de décompensation cardiaque. D/2005/10.273.35
25. Endoscopie par capsule. D2006/10.273.02.
26. Aspects médico-légaux des recommandations de bonne pratique médicale. D2006/10.273/06.
27. Qualité et organisation des soins du diabète de type 2. D2006/10.273/08.
28. Recommandations provisoires pour les évaluations pharmacoéconomiques en Belgique. D2006/10.273/11.
29. Recommandations nationales Collège d'oncologie : A. cadre général pour un manuel d'oncologie B. base scientifique pour itinéraires cliniques de diagnostic et traitement, cancer colorectal et cancer du testicule. D2006/10.273/13.
30. Inventaire des bases de données de soins de santé. D2006/10.273/15.
31. Health Technology Assessment : l'antigène prostatique spécifique (PSA) dans le dépistage du cancer de la prostate. D2006/10.273/18.
32. Feedback: évaluation de l'impact et des barrières à l'implémentation - Rapport de recherche: partie II. D2006/10.273/20.
33. Effets et coûts de la vaccination des enfants Belges au moyen du vaccin conjugué antipneumococcique. D2006/10.273/22.
34. Trastuzumab pour les stades précoces du cancer du sein. D2006/10.273/24.

35. Etude relative aux coûts potentiels liés à une éventuelle modification des règles du droit de la responsabilité médicale – Phase III : affinement des estimations. D2006/10.273/27.
36. Traitement pharmacologique et chirurgical de l'obésité. Prise en charge résidentielle des enfants sévèrement obèses en Belgique. D/2006/10.273/29.
37. Health Technology Assessment Imagerie par Résonance Magnétique. D/2006/10.273/33.
38. Dépistage du cancer du col de l'utérus et recherche du Papillomavirus humain (HPV). D/2006/10.273/36
39. Evaluation rapide de technologies émergentes s'appliquant à la colonne vertébrale : remplacement de disque intervertébral et vertébro/cyphoplastie par ballonnet. D/2006/10.273/39.
40. Etat fonctionnel du patient: un instrument potentiel pour le remboursement de la kinésithérapie en Belgique? D/2006/10.273/41.
41. Indicateurs de qualité cliniques. D/2006/10.273/44.
42. Etude des disparités de la chirurgie électorale en Belgique. D/2006/10.273/46.
43. Mise à jour de recommandations de bonne pratique existantes. D/2006/10.273/49.
44. Procédure d'évaluation des dispositifs médicaux émergents. D/2006/10.273/51.
45. HTA Dépistage du Cancer Colorectal : état des lieux scientifique et impact budgétaire pour la Belgique. D/2006/10.273/54.
46. Health Technology Assessment. Polysomnographie et monitoring à domicile des nourrissons en prévention de la mort subite. D/2006/10.273/60.
47. L'utilisation des médicaments dans les maisons de repos et les maisons de repos et de soins Belges. D/2006/10.273/62
48. Lombalgie chronique. D/2006/10.273/64.
49. Médicaments antiviraux en cas de grippe saisonnière et pandémique. Revue de littérature et recommandations de bonne pratique. D/2006/10.273/66.
50. Contributions personnelles en matière de soins de santé en Belgique. L'impact des suppléments. D/2006/10.273/69.
51. Besoin de soins chroniques des personnes âgées de 18 à 65 ans et atteintes de lésions cérébrales acquises. D/2007/10.273/02.
52. Rapid Assessment: Prévention cardiovasculaire primaire dans la pratique du médecin généraliste en Belgique. D/2007/10.273/04.
53. Financement des soins Infirmiers Hospitaliers. D/2007/10 273/06
54. Vaccination des nourrissons contre le rotavirus en Belgique. Analyse coût-efficacité D2007/10.273/10
55. Valeur en termes de données probantes des informations écrites de l'industrie pharmaceutique destinées aux médecins généralistes. D2007/10.273/13
56. Matériel orthopédique en Belgique: Health Technology Assessment. D2007/10.273/15.
57. Organisation et Financement de la Réadaptation Locomotrice et Neurologique en Belgique D/2007/10.273/19
58. Le Défibrillateur Cardiaque Implantable.: un rapport d'évaluation de technologie de santé D/2007/10.273/22
59. Analyse de biologie clinique en médecine général. D/2007/10.273/25

