

# Wetenschappelijk jaaroverzicht 2015



WETENSCHAPSCOMMISSIE

LEERHUIS

Albert Schweitzer  
ziekenhuis





# Woord vooraf

Hierbij presenteren wij u het wetenschappelijk jaaroverzicht 2015 van het Albert Schweitzer ziekenhuis (ASz). Als Topklinisch ziekenhuis (STZ) heeft het ASz wetenschap hoog op de agenda staan. Bijna alle vakgroepen zijn dan ook vertegenwoordigd in de Wetenschapscommissie. De Wetenschapscommissie zet het hele jaar door activiteiten in die bijdragen aan het stimuleren en faciliteren van het wetenschappelijk onderzoek. Een belangrijke doelstelling van 2015 was het schrijven van een nieuw meerjarenplan voor het ASz wetenschapsbeleid 2016-2019, velen in het ASz hebben hier hun bijdrage aan geleverd. Het komende jaar gaan we nog meer inzetten op het stimuleren en faciliteren van vooral langlopend en multidisciplinair onderzoek.

Dit jaaroverzicht is opgebouwd uit drie delen. In deel een wordt een overzicht gepresenteerd van de wetenschappelijke activiteiten die dit jaar zijn georganiseerd door de Wetenschapscommissie. In het tweede deel van dit overzicht vindt u per afdeling de publicaties die in PubMed zijn terug te vinden (met affiliatie Albert Schweitzer ziekenhuis). In het derde deel geven we de overige wetenschappelijke output van het jaar 2015 per afdeling weer.

Wetenschap doe je samen, multidisciplinair en multicenter. In een wetenschappelijk klimaat waarbij dit steeds belangrijker wordt, is het mooi om te zien dat de activiteiten die we als Wetenschapscommissie inzetten hiertoe bijdragen. De wetenschapsbijeenkomsten worden goed bezocht, door onderzoekers uit de diverse vakgroepen en diverse disciplines. De ASz onderzoekers hebben zich naast hun klinische taak, ook dit jaar zich weer met passie ingezet voor wetenschap. Onderzoek werd verricht en gepresenteerd op nationale en internationale congressen. Het aantal PubMed publicaties is dit jaar stabiel gebleven in vergelijking met het jaar 2014. De meeste publicaties van het ASz worden geproduceerd door de afdelingen Chirurgie, Interne Geneeskunde, Pathologie en Radiologie.

Het wetenschappelijk jaaroverzicht 2015 is tot stand gekomen door de bijdragen van de ASz onderzoekers die naast hun klinische zorg, een bijdrage aan verbetering van de gezondheidszorg geven door wetenschappelijk onderzoek te verrichten. We willen iedereen hartelijk bedanken voor hun inzet en het mogelijk maken van dit jaaroverzicht.

Namens de Wetenschapscommissie,

*Joke Bosch, wetenschapscoördinator wetenschapsbureau*  
*Jurgen Riedl, voorzitter wetenschapscommissie*

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# Samenstelling Wetenschapscommissie 2015

## Dagelijks bestuur

Dr. J. Riedl, voorzitter, klinisch chemicus  
Dr. M-D Levin, vicevoorzitter, internist-hematoloog (tot 1/8/2015)  
Dr. P.E. Westerweel, vicevoorzitter, internist-hematoloog (vanaf 1/8/2015)  
Dr. J.L. Bosch, wetenschapscoördinator, klinisch epidemioloog  
Drs. A.D. Klaren, manager leerhuis & kwaliteit, veiligheid en innovatie  
Mw. E.Y. de Kruyf, secretariaat

## Leden wetenschapscommissie

Drs. M.M. Beex – Oosterhuis, ziekenhuisapotheker  
Dr. E.F.H. van Bommel, internist-nefroloog  
Dr. D. Cheung, longarts  
Drs. L.P.L.H. Cuijpers, klinisch psycholoog  
Dr. D. Dickerscheid, klinisch fysicus  
Dr. H.M.E. Frenay, arts-microbioloog  
Drs. I Geelen, arts assistent interne geneeskunde  
Drs. E. Groot, geriater  
Mw. K. Hamelink, IC verpleegkundige  
Mw. R. van Hof, medisch informatiespecialist  
Dr. M.C.J.M. Kock, radioloog  
Dr. M Kofflard, cardioloog  
Dr. W. Lok, KNO arts  
Dr. B. Maraha, arts microbioloog  
Dr. A.C. de Mol, kinderarts  
Dr. P.W. Plaisier, chirurg  
Dr. N. van Putte – Katier, radioloog  
Drs. J.M.M. van de Ridder, adviseur medische vervolopleidingen leerhuis (tot en met september 2015)  
Drs. S. Rombout - de Weerd, gynaecoloog  
Dr. T.C.J. Sas, kinderarts  
Drs. A.M.J.V. Schyns – van den Berg intensivist-anesthesioloog  
Drs. S. Slegers, arts assistent klinische fysica  
Statisticus ErasmusMC (Dr. J. van Rosmalen)  
Dr. N.B. Swarte, gynaecoloog  
Drs. T.A.G. Tijssen, ziekenhuisapotheker  
Drs. E.M. de Vogel, ziekenhuisapotheker  
Dr. P.J. Westenend, patholoog  
Drs. M. Willeboer, spoedeisende hulp arts  
Dr. F.H.J. Wolfhagen, MDL arts  
Dr. D. Zemel, neuroloog

### **Hoofdredactie wetenschappelijk tijdschrift 'WASz'**

Drs. S. Slegers, arts assistent klinisch fysisus

Drs. I. Geelen, arts assistent interne geneeskunde

Dr. M.C.J.M. Kock, radioloog



# **Deel I**

## **Wetenschappelijk jaarverslag Wetenschapscommissie 2015**

## Wetenschapscommissie

De Wetenschapscommissie van het ASz heeft als doel het medisch wetenschappelijk onderzoek te ondersteunen, te stimuleren en om een breed gedragen goed onderbouwd wetenschapsbeleid te maken. De commissie werkt hierbij nauw samen met het Wetenschapsbureau.

De Wetenschapscommissie en het Wetenschapsbureau zijn met diverse andere commissies en groepen actief om wetenschap te bevorderen, zoals de bibliotheek, de lokale toetsingscommissie (WOAC), de fondsenwerver, de afdeling Communicatie en de Medisch Specialistische OpleidingsCommissie (MSOC).

In 2009 werd de Wetenschapscommissie opgericht om een bredere basis te leggen voor het wetenschappelijke onderzoek in het ASz. Bijna iedere afdeling van ons ziekenhuis participeert binnen de Wetenschapscommissie. Een jaar later (2010) werd een dagelijks bestuur gevormd, bestaande uit twee specialisten en vertegenwoordiging uit het Wetenschapsbureau en het Leerhuis, welke maandelijks vergaderen. Voor statistisch onderwijs en ondersteuning werden statistici van de afdeling Biostatistiek van het Erasmus MC aangesteld (2012) voor een dag in de week. Sinds 2014 is er een klinisch epidemioloog aangesteld als wetenschapscoördinator. Dit jaar is het nieuwe meerjarenplan ASz wetenschapsbeleid 2016-2019 geschreven.

### Meerjarenplan ASz Wetenschapsbeleid 2016-2019

Het meerjarenplan ASz Wetenschapsbeleid 2016-2019 is een voortzetting op het beleidsplan 2011-2015 en richt zich wederom op het verder verbeteren en bevorderen van het onderzoeksklimaat in het ASz. Het volgt de ontwikkelingen in het wetenschapsklimaat, waarbij meer nadruk gelegd zal worden op multidisciplinair en multicenter samenwerken om de kans op implementatie te vergroten en zodoende echt een verschil te maken in het vernieuwen en verbeteren van patiëntenzorg.

Op 14 september jl. werd een 'heidag' georganiseerd om samen terug te kijken en de richting te bepalen voor de komende jaren. De avond werd begeleid door Hans Wijlens van Zenith Training. De groep bestond uit een afvaardiging van de Wetenschapscommissie, de lokale toetsingscommissie (WOAC), het Wetenschapsbureau, de afdeling Innovatie, het Leerhuis, de Medisch Specialistische OpleidingsCommissie (MSOC), de Arts-Assistenten Vereniging (AAV), het Medisch Staf Bestuur (MSB) en natuurlijk de onderzoekers (verpleegkundig en medisch) zelf. Vervolgens is de input door de wetenschapscoördinator samen met het dagelijks bestuur van de Wetenschapscommissie verder uitgewerkt in het meerjarenplan.

De visie op wetenschap in het ASz voor de komende jaren is als volgt geformuleerd:

*“In het Albert Schweitzer ziekenhuis willen we een hoogwaardige speler en partner zijn voor wetenschappelijk onderzoek. Het wetenschappelijk onderzoek zal zich hierbij focussen op langlopende onderzoekslijnen die multidisciplinair zijn. De onderzoekslijnen bevatten onderzoeksvragen die zich richten op zowel medische, verpleegkundige, als paramedische vraagstukken. Door vanuit de verschillende perspectieven in een onderzoekslijn samen te werken, wordt het thema verdiept en wordt de kwaliteit van onderzoek verbeterd en de kansen op implementatie, onderzoeksgelden en publicaties vergroot. Bovendien werkt het inspirerend en is het leuker om samen onderzoek te doen. Om bovengenoemde redenen is het daarom ook van belang dat multicenter wordt samengewerkt. De focus van wetenschap in de onderzoekslijnen dient een afspiegeling te zijn van de zorg en speerpunten waar het ASz voor staat. Het stimuleren van speerpuntonderzoek past hierin; doen waar je goed in bent.”*

De vergaderdata in 2015 van de voltallige Wetenschapscommissie waren op de dinsdagen 17 maart, 2 juni, 27 oktober en 1 december.

Het dagelijks bestuur van de Wetenschapscommissie kwam in 2015 15 keer bijeen. De vergaderdata waren op de volgende dinsdagen: 20 januari, 9 februari, 10 maart, 7 en 21 april, 12 mei, 2 en 16 juni, 7 juli, 25 augustus, 29 september, 20 oktober, 17 november en 6 december.

## Albert Schweitzer Stipendium

In 2010 is het Albert Schweitzer Stipendium in het leven geroepen. Dit stipendium is bedoeld voor patiëntgebonden, klinisch onderzoek dat wordt uitgevoerd door ASz onderzoekers in het ASz. Het biedt onderzoekers de mogelijkheid een tegemoetkoming in onderzoekskosten te krijgen.

De stipendiumaanvragen kunnen een- tot tweejaarlijks worden ingediend, afhankelijk van het stipendium budget en de hoeveelheid aanvragen. Het indienen en beoordelen van deze projecten verloopt volgens een vaste procedure. Doel van deze procedure is om de rechtsgelijkheid tussen indieners te garanderen, de transparantie van de beoordeling te vergroten en een vergelijking met subsidieprocedures elders mogelijk te maken. De Wetenschapscommissie toetst de aanvragen die voor subsidiëring in aanmerking wensen te komen op transparante wijze.

Voor de stipendia 2015, werd een budget van bijna €100.000 toegekend.

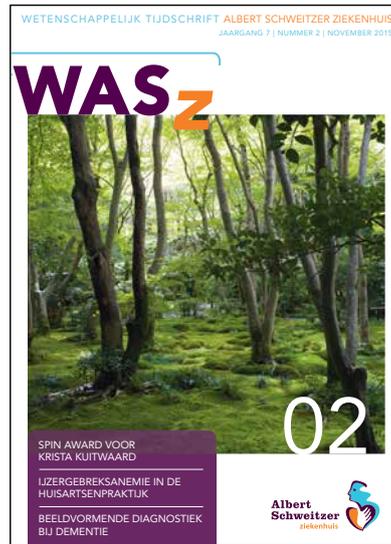
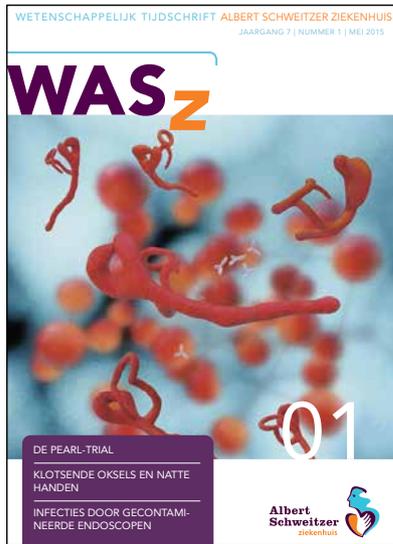
2015	Vakgroep	Aanvraag	Titel onderzoek
	Chirurgie	Carolien Drukker	Risico op locoregionaal recidief na mammasparende chirurgie voor de behandeling van ductaal carcinoma in situ
	Interne Geneeskunde	Hanah Rier	HERBAS
	Radiologie	Ineke Dams	Clinical value of mid-term and long-term follow-up histopathologic benign microcalcifications after vacuum-assisted stereotactic biopsy in the breast
	Resultlab	Karlijn Stouten	Een evidence-based algoritme voor de diagnose van de oorzaak van anemie
	Interne Geneeskunde	Inge Geelen	Molucare respons monitoring in nieuwe behandelde CML patiënten: voldoende betrouwbaar als enkel criterium of is routinematig cytogenetisch onderzoek nog altijd noodzakelijk?
	Neurologie	Elles Zock	MRI-vessel wall imaging in young stroke patiënten
	Intensive Care	Ralph So	De invloed van vroege identificatie van en respons op klinische achteruitgang van patiënten op de verpleegafdeling Heelkunde door het gebruik van continue automatische patiëntenmonitoring op patiëntgerelateerde uitkomsten
	Interne Geneeskunde	Sylvia Sprangers	Onderzoek naar het Gebruik van een Langdurig Orale oncolytica behandeling bij de (hema)oncologie patiënt binnen het Albert Schweitzer ziekenhuis (GLOBAS)

### Extra Verpleegkundig Albert Schweitzer Stipendium voor Wetenschappelijk Verpleegkundig onderzoek.

De Raad van Bestuur heeft dit jaar een speciale stipendium ronde uitgeschreven van € 25.000 voor wetenschappelijk verpleegkundig onderzoek. Dit stipendium is toegekend aan verpleegkundig specialist Sylvia Sprangers van de afdeling Interne Geneeskunde. Zij doet onderzoek binnen het GLOBAS-project. Dit staat voor **G**ebruik **L**angdurige **O**rale oncolytica **B**ehandeling in het **A**lbert **S**chweitzer ziekenhuis. Ze werkt hiervoor nauw samen met apotheker Madelinde Vaane, verpleegkundige Ingrid Steenis en internist-hematologen Peter Westerweel en Mark-David Levin. Op de lange termijn hoopt ze op dit onderzoek te kunnen promoveren.

## Wetenschappelijk tijdschrift 'WASz'

Het wetenschapstijdschrift Wasz (oplage 1000 ex.) verschijnt twee keer per jaar in de reguliere vorm. De derde uitgave is gewijd aan abstracts van de wetenschapsdag. Het WASz is bedoeld om medewerkers, verwijzers en andere geïnteresseerden op de hoogte te houden van de wetenschappelijke activiteiten in het Albert Schweitzer ziekenhuis. De kosten worden volledig gedragen door de advertentieopbrengsten.



## Cursussen

De volgende cursussen zijn aangeboden in 2015

Scholing	Door wie	Frequentie	Totaal aantal deelnemers
Good Clinical Practice	Externe partij: TAPAS	5x per jaar	57
Wetenschappelijk schrijven in het Engels	Externe partij: Text en training	2x per jaar, 6 bijeenkomsten per reeks	22
Cursus poster maken	Leerhuis: Onderwijskundige	1 keer per jaar	9
Literatuur referenties (Refworks)	Bibliotheek: Medisch informatie specialist	Op aanvraag	10
PubMed	Bibliotheek: Medisch informatie specialist	Op aanvraag	15

## Wetenschapslunch

Elke vierde dinsdag in de maand (m.u.v. de maand juni waarin de wetenschapsdag wordt georganiseerd en de vakanties) wordt de wetenschapslunch georganiseerd waarbij een onderzoeker zijn of haar lopend onderzoek presenteert en zijn of haar ervaringen deelt op dit gebied. De wetenschapslunch biedt onderzoekers een informeel platform om, van elkaar te leren, opbouwende kritiek te leveren en om interdisciplinaire samenwerking te stimuleren.

In 2015 vonden de volgende presentaties plaats

Datum	Onderwerp	Spreker-vakgroep
27-01-2015	Anemia in de eerste lijn: oorzaken en overleving	Karlijn Stouten - Klinische chemie/ Resultlab
24-03-2015	Promotie-onderzoek 'Prognostic and predictive biomarkers in colorectal cancer'; resultaten, ervaringen, knelpunten en toekomstplannen	Marlies Reimers - Aios radiologie
26-05-2015	PHAROS-CML: retrospectief cohort onderzoek naar CML in Nederland	Inge Geelen - AIOS interne geneeskunde
22-09-2015	Korte presentaties ASz stipendia onderzoek	Stipendia ronde 2015 ontvangers
27-10-2015	Longmetastasen	Erik von Meyenfeldt - (Long)Chirurgie
24-11-2015	MAC-studie	Kathleen Welborn - Kindergeneeskunde Miranda de Jong - Kindergeneeskunde

## ASz Promovendi Netwerk

Promoveren in het ASz betekent dat je een zogenaamde buitenpromovendus bent en een samenwerkingsverband hebt met een universitair medisch centrum. Dit is wezenlijk anders dan promoveren met een aanstelling aan een universiteit. Om onze promovendi beter te kunnen begeleiden en ondersteunen zijn we dit jaar gestart met een promovendi netwerk met als doel dat ASz-promovendi elkaar leren kennen en weten te vinden. Het opdoen van nuttige contacten en het uitwisselen van ervaringen staat hierbij voorop. De bijeenkomst is informeel en informatief van karakter. De promovendi kunnen zelf een thema aandragen. De bijeenkomsten worden begeleid door de wetenschapscoördinator (voorheen universitair hoofddocent), die ruime ervaring heeft in het opleiden van promovendi. Het Leerhuis ondersteunt en faciliteert deze netwerkbijeenkomsten.

## Ondersteuning onderzoek

Naast bovengenoemde activiteiten vindt individuele ondersteuning plaats door een klinisch epidemioloog en statisticus. De statistici uit het Erasmus MC, die elke dinsdag aanwezig zijn, hebben dit jaar meer dan 130 consulten verricht bij meer dan 15 verschillende afdelingen. De onderwerpen zijn zeer divers zoals power berekeningen, mixed effect modellen, competing risks, en evaluatie van diagnostische testen.

## Toetsing en registratie studies

Het ASz heeft een Wetenschappelijk Onderzoek Advies Commissie (WOAC). De WOAC beoordeelt de bij haar ingediende wetenschappelijke onderzoeken (trials) op de lokale uitvoerbaarheid in het ziekenhuis en brengt hierover advies uit aan de Raad van Bestuur.

Sinds 2012 is de richtlijn 'Externe Toetsing' (RET 2012) van kracht. WMO-plichtige trials worden door de erkende toetsingscommissie medisch-ethisch getoetst. Bij goedkeuring worden deze trials door de WOAC lokaal getoetst op haalbaarheid. Het invullen van de gestandaardiseerde controlelijst beoordelingscriteria lokale uitvoerbaarheid (STZ) is daarbij van belang. Medisch-wetenschappelijk onderzoek geïnitieerd in het ASz en niet vallend onder de WMO wordt wel medisch-ethisch en op lokale uitvoerbaarheid door de WOAC beoordeeld.

De commissie werkt volgens een reglement. De commissie heeft een eigen site op intranet waar het reglement en de relevante informatie voor onderzoekers is te vinden.

De WOAC behandelde in 2015, 85 trials voor wetenschappelijk onderzoek. Hiervan waren 25 trials door specialisten/medewerkers van het ASz zelf geïnitieerd. Van de 85 trials zijn 37 WMO plichtig en 48 niet WMO plichtig, 28 trials waren gesponsorde trials.

De Raad van Bestuur heeft – gehoord hebbende het advies van de WOAC – een lokale uitvoerbaarheidsverklaring voor deze trials afgegeven. (Zie document Jaarverslag Wetenschappelijk Onderzoek Advies Commissie 2015) .

## Overige activiteiten

De wetenschapscoördinator en/of de voorzitter van de Wetenschapscommissie heeft ten behoeve van interne en externe relaties dit jaar regelmatig overleg gehad met onder andere de Raad van Bestuur, Medisch Staf Bestuur (MSB), Wetenschappelijk Onderzoek Advies Commissie (WOAC), Medisch Specialistische OpleidingsCommissie (MSOC) en Verpleegkundige Advies Raad (VAR). Daarnaast is de wetenschapscoördinator vertegenwoordigd in het STZ netwerk wetenschapscoördinatoren, is lid van de STZ werkgroep GCP/Brok scholing en neemt zitting in de adviesraad van de Amstel Academi voor vervolgopleiding research verpleegkundige.

## Wetenschapsdag 2015

Op 18 juni jl. vond de 11e Wetenschapsdag plaats in het Auditorium van het ASz. De wetenschapsdag werd bezocht door meer dan 80 deelnemers van diverse afdelingen uit het ziekenhuis. Het programma was zeer gevarieerd. Plenair werden 10 mondelinge presentaties en 13 korte posterpresentaties gegeven.

De prijs voor beste publicatie werd uitgereikt aan Nienke van Putte-Katier (radioloog) met het artikel "Mesenteric panniculitis: prevalence, clinoradiological presentation and 5-year follow-up". Auteurs: N. Van Putte-Katier, E.F.H. van Bommel, O.E. Elgersma, T.R. Hendrsz. Gepubliceerd in het British Journal of Radiology (2014; 87: 20140451).



De prijs voor de beste mondelinge presentatie ging naar Elles Zock (Physician Assistant Neurologie) met de presentatie getiteld: "Help-seeking behaviour and onset-to-alarm time after stroke", en de beste posterpresentatie werd gegeven door Miranda Wiggelinkhuizen (AIOS kindergeneeskunde) met de titel: "Gebruik van e-mail en WhatsApp door artsen vormt bedreiging voor veiligheid patiëntgegevens".



## Mondelinge presentaties tijdens de wetenschapsdag 2015

Abstract titel	Specialisme	Inzending
"Survival of patients with Her2 positive metastatic breast cancer after failure of adjuvant treatment with trastuzumab"	Interne Geneeskunde	Hanah Rier
"Anaemia and mortality in patients presenting to the general practitioner"	Resultlab	Karlijn Stouten
"Wordt eerder ontslag naar huis met voeding via sonde bij prematuren <37 weken de nieuwe standaard?"	Kindergeneeskunde	Francoise van Kampen
"Cutaneous mitochondrial PO2 is an early indicator of the physiological limit of hemodilution in the pig"	Anesthesie	Luuk Römers
"Underestimate rates and upgrading in patients with a needle biopsy diagnosis DCIS in the Netherlands"	PAL	Pieter Westenend
"Two-year Follow-up of GLP-1 analogues and Insulin in Clinical Practice"	Interne Geneeskunde	Evert van Velsen
"The C-vies study, To evaluate whether conventional 2D mammography can be omitted when performing 3D tomosynthesis with 2D synthesised mammography"	Radiologie	Evert Jan van Dijk
"Help-seeking behaviour and onset-to-alarm time after stroke"	Neurologie	Elles Zock
"De PEARL-trial, een onderzoek naar de veiligheid en toepasbaarheid van de Drug Eluting Balloon (DEB)"	Cardiologie	Anne Geert van Driel
"The effect of early identification of and response to clinically deteriorating patients on the surgical ward by using automated continuous patient monitoring on mortality: is there a "weekend effect" ?	Intensive Care	Ralph So

## Posterpresentaties tijdens de wetenschapsdag 2015

Poster titel	Specialisme	Inzending
Perioperative Transfusion Study (PETS): does a liberal transfusion protocol improve outcome in high-risk cardiovascular patients undergoing non-cardiac surgery?	Anesthesie	Samir Ali
Besluitvorming en voorlichting over de ICD in de laatste levensfase	Cardiologie	Anne Geert van Driel
The role of fibrinogen in massive postpartum hemorrhage, a case report	Gynaecologie	Minke van Minde
Green urine in the ICU	Intensive Care	Leo te Velde
Mini-audit of the afferent limb of rapid response system: an evaluation of nursing practice on surgical and medical patients during both weekdays and weekends	Intensive Care	Ralph So
The impact of implementing a rapid response system: a comparison of cardio- pulmonary arrests and mortality among two clinical locations of a large teaching hospital in the Netherlands	Intensive Care	Ralph So
Adherence to national guideline in newly discovered anemia of chronic disease in general practice	Interne Geneeskunde	Annemarie Schop
GLOBAS	Interne Geneeskunde	Sylvia Sprangers
Gebruik van e-mail en WhatsApp door artsen vormt bedreiging voor veiligheid patiëntgegevens	Kindergeneeskunde	Miranda Wiggelinkhuizen
Improvement sepsis outcome in a large hospital organisation: "Take your time and invite other professions to help you"	SEH	Erick Oskam
Remifentanil use for procedural sedation and analgesia in the emergency department	SEH	Martijn van Hooft/ Roos America
Is Rapydan® superieur aan Emla® als lokaal anestheticum bij kinderen?	Ziekenhuisapotheek	Julie Erkelens
Hoe kunnen hoge clozapinespiegels worden verklaard en welke acties worden ondernomen door de behandelaar en ziekenhuisapotheeker?	Ziekenhuisapotheek	Marloes Overbeeke

## **Deel II**

# **PubMed publicaties 2015**

Per vakgroep

## PubMed publicaties 2015

### Per vakgroep

In onderstaande tabel staan het aantal PubMed publicaties die in de afgelopen drie jaar door een of meer van onze professionals van het Albert Schweitzer ziekenhuis zijn gepubliceerd.

Tabel Aantal Pubmed publicaties in het ASz

Aantal PubMed publicaties*	2013	2014	2015
<b>Specialisme **</b>			
Anesthesiologie	3	9	6
Cardiologie	7	7	6
Chirurgie	15	18	14
Dermatologie	4	4	3
Gynaecologie	5	8	5
Interne Geneeskunde	12	10	10
Keel-, Neus- en Oorheelkunde		1	1
Kindergeneeskunde	6	10	5
Klinische Chemie	2	4	3
Klinische Fysica		2	1
Leerhuis		1	2
Longgeneeskunde			2
MDL-geneeskunde	3	3	5
Medische Microbiologie	5	8	6
Neurochirurgie	1		
Neurologie	3	2	4
Nuclaire Geneeskunde			1
Oogheelkunde	1	1	
Orthopedie			
Ouderengeneeskunde			1
Pathologie	8	10	12
Plastische Chirurgie			2
Psychiatrie			1
Radiologie	6	15	13
Reumatologie	1	3	4
Spoedeisende Geneeskunde	1		
Urologie		1	
Ziekenhuisapotheek	1	1	

\* Voor de verantwoording van de getallen verwijzen we naar de paragraaf verantwoording van dit jaaroverzicht.

\*\* Als meerdere afdelingen zijn betrokken bij een publicatie wordt deze publicatie bij de betreffende afdelingen weergegeven.

# Anesthesiologie

## Cell Salvage in Hip and Knee Arthroplasty: A Meta-Analysis of Randomized Controlled Trials.

van Bodegom-Vos L1, Voorn VM1, So-Osman C2, Vliet Vlieland TP3, Dahan A4, **Koopman-van Gemert AW5**, Vehmeijer SB6, Nelissen RG3, Marang-van de Mheen PJ1. *J Bone Joint Surg Am.* 2015 Jun 17;97(12):1012-21. doi: 10.2106/JBJS.N.00315.

**BACKGROUND:** Cell salvage is used to reduce allogeneic red blood-cell (RBC) transfusions in total hip arthroplasty (THA) and total knee arthroplasty (TKA). We performed a meta-analysis to assess the effectiveness of cell salvage to reduce transfusions in THA and TKA separately, and to examine whether recent trials change the conclusions from previous meta-analyses.

**METHODS:** We searched MEDLINE through January 2013 for randomized clinical trials evaluating the effects of cell salvage in THA and TKA. Trial results were extracted using standardized forms and pooled using a random-effects model. Methodological quality of the trials was evaluated using the Cochrane Collaboration's tool for risk-of-bias assessment.

**RESULTS:** Forty-three trials (5631 patients) were included. Overall, cell salvage reduced the exposure to allogeneic RBC transfusion in THA (risk ratio [RR], 0.66; 95% confidence interval [CI], 0.51 to 0.85) and TKA (RR, 0.51; 95% CI, 0.39 to 0.68). However, trials published in 2010 to 2012, with a lower risk of bias, showed no significant effect of cell salvage in THA (RR, 0.82; 95% CI, 0.66 to 1.02) and TKA (RR, 0.91; 95% CI, 0.63 to 1.31), suggesting that the treatment policy regarding transfusion may have changed over time.

**CONCLUSIONS:** Looking at all trials, cell salvage still significantly reduced the RBC exposure rate and the volume of RBCs transfused in both THA and TKA. However, in trials published more recently (2010 to 2012), cell salvage reduced neither the exposure rate nor the volume of RBCs transfused in THA and TKA, most likely explained by changes in blood transfusion management.

**LEVEL OF EVIDENCE:** Therapeutic Level I. See Instructions for Authors for a complete description of levels of evidence.

PMID: 26085536

## Coaching Reduced the Radiation Dose of Pain Physicians by Half during Interventional Procedures.

**Slegers AS1, Gültuna I, Aukes JA, van Gorp EJ, Blommers FM, Niehof SP, Bosman J.** *Pain Pract.* 2015 Jun;15(5):400-6. doi: 10.1111/papr.12251. Epub 2014 Oct 29.

The increased use of C-arm fluoroscopy in interventional pain management has led to higher radiation exposure for pain physicians. This study investigated whether or not real-time radiation dose feedback with coaching can reduce the scatter dose received by pain physicians. Firstly, phantom measurements were made to create a scatter dose profile, which visualizes the average scatter radiation for different C-arm positions at 3 levels of height. Secondly, in the clinical part, the radiation dose received by pain physicians during pain treatment procedures was measured real-time to evaluate (1) the effect of real-time dose feedback on the received scatter dose, and (2) the effect of knowledge of the scatter dose profile and active coaching,

on the scatter dose received by the pain physician. The clinical study included 330 interventional pain procedures. The results showed that real-time feedback of the received dose did not lead to a reduction in scatter radiation. However, visualization of the scatter dose in a scatter dose profile and active coaching on optimal positions did reduce the scatter radiation received by pain physicians during interventional pain procedures by 46.4% (P = 0.05). Knowledge of and real-time coaching with the scatter dose profile reduced the dose of pain physicians by half, caused by their increased awareness for scatter radiation and their insight into strategic positioning.

PMID: 25354342

### **Incidence of alloantibody formation after ABO-D or extended matched red blood cell transfusions: a randomized trial (MATCH study).**

Schonewille H1,2, Honohan Á1,2, van der Watering LM1,2, Hudig F3, Te Boekhorst PA4, **Koopman-van Gemert AW5**, Brand A2,6.

Transfusion. 2016 Feb;56(2):311-20. doi: 10.1111/trf.13347. Epub 2015 Oct 7.

**BACKGROUND:** Most incidentally transfused patients receive only ABO-D-compatible transfusions and antibodies are formed in up to 8%. The effect of extended (c, C, E, K, Fya, Jka, and S antigens) matched (EM) and ABO-D-matched red blood cell (RBC) transfusions on the incidence of new clinically relevant RBC antibody formation after a first elective transfusion event in surgical patients was studied.

**STUDY DESIGN AND METHODS:** A multicenter randomized trial was performed in nontransfused patients who were scheduled to experience a single elective transfusion event of maximal 4 RBC units. The primary outcome was the incidence of newly formed warm reacting clinically relevant RBC alloantibodies measured in three follow-up (FU) samples taken at 7 to 10 days, 4 to 6 weeks, and 4 to 6 months posttransfusion. **RESULTS:** A total of 853 patients were randomized, and of these, 333 patients were transfused with a total of 1035 RBC units. At least one FU sample was available from 97% of transfused patients. In intention-to-treat analysis, new antibodies were detected in 10 of 155 ABO-D and seven of 178 EM patients, respectively. Per-protocol analysis including 190 patients showed a nonsignificant absolute risk difference (ARD) of 5.3% (95% confidence interval [CI], -1.4% to 12%) in alloimmunization between study arms. In a post hoc analysis of 138 patients who received RBCs but no platelet (PLT) transfusions the ARD increased to significance, 8.0% (95% CI, 0.4-16.0).

**CONCLUSION:** Extended matching for selected antigens reduced the alloimmunization risk by 64% in surgical patients. Extended matching seems successful only if the patient did not receive accompanying nonmatched PLT transfusions.

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PMID: 26442648

### **Nonelective surgery at night and in-hospital mortality: Prospective observational data from the European Surgical Outcomes Study.**

van Zaane B, van Klei WA, Buhre WF, Bauer P, Boerma EC, Hoeft A, Metnitz P, Moreno RP, Pearse R, Pelosi P, Sander M, Vallet B, Pettilä V, Vincent JL, Rhodes A; European Surgical Outcomes Study (EuSOS) group for the Trials groups of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology. **Koopman-van Gemert AWMM** een van de auteurs.

Eur J Anaesthesiol. 2015 Jul;32(7):477-85. doi: 10.1097/EJA.000000000000256. PubMed

PMID: 26001104.

### **Postcaesarean section analgesia: are opioids still required?**

**Schyns-van den Berg AM1**, Huisjes A, Stolker RJ.

Curr Opin Anaesthesiol. 2015 Jun;28(3):267-74. doi: 10.1097/ACO.000000000000195.

**PURPOSE OF REVIEW:** The use of opioids for postoperative pain relief after caesarean section is widely spread. Because of unwanted well known side-effects, alternative drugs and methods of pain relief have been introduced, either in addition to or instead of opioids. Can postcaesarean analgesia be achieved these days without opioids?

**RECENT FINDINGS:** Most components of multimodal postcaesarean analgesia have not been studied thoroughly during pregnancy and lactation, and not one or a combination of them has yet proven to be superior to opioids. New applications of local anaesthetics and other drugs, new combinations of existing drugs and new developments in predicting an individual's response to pain provide tools to minimize opioid use for postoperative pain relief in caesarean section.

**SUMMARY:** The dependency on opioids for postcaesarean analgesia is diminishing, but in order to develop effective, well tolerated alternatives, more research is needed. In the meantime, opioids are here to stay.

PMID: 25887195

### **Subcutaneous Stimulation as an Additional Therapy to Spinal Cord Stimulation for the Treatment of Low Back Pain and Leg Pain in Failed Back Surgery Syndrome: Four-Year Follow-Up.**

**Hamm-Faber TE1, Aukes H, van Gorp EJ, Gültuna I.**

Neuromodulation. 2015 May 6. doi: 10.1111/ner.12309. [Epub ahead of print]

**OBJECTIVE:** The objective of this study is to investigate the efficacy of long-term follow-up of subcutaneous stimulation (SubQ) as an additional therapy for patients with failed back surgery syndrome (FBSS) with chronic refractory pain, for whom spinal cord stimulation (SCS) alone was unsuccessful in treating low back pain.

**STUDY DESIGN:** Prospective case series.

**MATERIALS AND METHODS:** FBSS patients with leg and/or low back pain whose conventional therapies had failed, received a combination of SCS (8-contact Octad lead, 3877-45 cm, Medtronic, Minneapolis, MN, USA) and/or SubQ (4-contact Quad Plus lead (s), 2888-28 cm, Medtronic). Initially, an Octad lead was placed in the epidural space for SCS for a trial stimulation to assess the suppression of leg and/or low back pain. Where SCS alone was insufficient in treating low back pain, lead(s) were placed superficially in the subcutaneous tissue of the lower back, exactly in the middle of the pain area. A pulse generator (Prime Advanced,

37702, Medtronic) was implanted if the patient reported more than 50% pain relief during the trial period. We investigated the long-term effect of neuromodulation on pain with the visual analog scale (VAS), and disability using the Quebec Pain Disability Scale. The results after 46 months are presented.

**RESULTS:** Eleven patients, five men and six women (age  $51 \pm 8$  years, mean  $\pm$  SD) were included in the pilot study. In nine cases, SCS was used in combination with SubQ leads. Two patients received only SubQ leads. In one patient, the SCS + SubQ system was removed after nine months and these results were not taken into account for the analysis. Baseline scores for leg (N = 8) and low back pain (N = 10) were VASbl:  $59 \pm 15$  and VASbl:  $63 \pm 14$ , respectively. The long-term follow-up period was  $46 \pm 4$  months. SCS significantly reduced leg pain after 12 months (VAS12:  $20 \pm 11$ ,  $p_{12} = 0.001$ ) and 46 months (VAS46:  $37 \pm 17$ ,  $p_{46} = 0.027$ ). Similarly, SubQ significantly reduced back pain after 12 months (VAS12:  $33 \pm 16$ ,  $p_{12} = 0.001$ ) and 46 months (VAS46:  $40 \pm 21$ ,  $p_{46} = 0.013$ ). At 12 months, the Quebec Pain Disability Scale (QPDS) was  $49 \pm 12$  and after 46 months,  $53 \pm 15$ . Both at 12 and 46 months, the QPDS values were statistically significantly better ( $p_{12} = 0.001$ ,  $p_{46} = 0.04$ ) compared with baseline values (QPDSbl:  $61 \pm 15$ ). In one patient, the pain suppressive effect of SCS/SubQ had disappeared completely over time and the pain scores returned to prestimulation values. In four, patients back pain scores increased over time due to new issues (SI-joint problems, degenerative spine problems, disc problems, and hip pain) unrelated to FBSS and for which SCS/SubQ was not targeted or a reason for implantation at the start of the pilot study.

**DISCUSSION:** This is the first prospective report on the combined use of SCS and SubQ with a follow-up period of four years. These data show that SCS and/or SubQ provide persistent long-term pain relief for leg and back pain in patients with FBSS. One should also take into account that new back/leg pain problems may evolve over time and increase the pain score which impact overall pain treatment.

**CONCLUSION:** SCS combined with SubQ can be considered an effective long term treatment for low back pain in patients with FBSS for whom SCS alone is insufficient in alleviating their pain symptoms.

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**KEYWORDS:** Chronic pain; failed back surgery syndrome; low back pain; peripheral nerve field stimulation; subcutaneous stimulation

PMID: 25943093

## **A curly case: dissecting giant arteriovenous anomaly - left main coronary artery shunting to superior vena cava.**

**de Mulder M1, Hendriksz TR, de Jong PL, IJsselmuiden AJ.**

EuroIntervention. 2015 Oct 22;11(6):e1. doi: 10.4244/EIJV11I6A132.

PMID: 26499049

## **A 'foreign' body.**

**van Gameren M1, van Gent MW2, Kock MC3, van den Bos EJ2, Kofflard MJ2.**

Eur Heart J Cardiovasc Imaging. 2015 Dec 24. pii: jev334. [Epub ahead of print]

PMID: 26705486

## **Ischemic cardiomyopathy and cerebral infarction in a young patient associated with khat chewing.**

**Meulman TJ1, Bakker J1, van den Bos EJ2.**

Case Rep Radiol. 2015;2015:893176. doi: 10.1155/2015/893176. Epub 2015 Feb 26.

Khat is a stimulating agent used by many people in the Horn of Africa and the Arabian peninsula. Khat chewing is a known cardiovascular risk factor and is thought to cause vasoconstriction, systemic hypertension, and thrombogenicity. A 33-year-old Somali man initially presented with loss of neurological function of the left arm, hazy vision, and headache. He smokes tobacco and chews two bundles of khat a week for more than 10 years. His ECG on admission showed a Q wave in V1 and V2 and 2mm ST-elevations in V1, V2, and V3 and a terminal negative T wave in I, aVL, V2, V3, and V4, consistent with a recent, evolving anterior infarction. A noncontrast enhanced CT of the brain showed ischemia in the right middle cerebral artery vascular territory. An MRI showed recent ischemia in the vascular territory of the posterior division of the right middle cerebral artery. Coronary angiography showed a 70% stenosis with haziness of the proximal left anterior descending artery. Diagnostic tests and imaging are consistent with recent myocardial infarction in the LAD vascular territory because of coronary spasm and cerebral infarction in the middle cerebral artery vascular territory probably related to khat chewing.

PMID: 25815235

**One-year clinical outcomes of the STENTYS Self-Apposing<sup>®</sup> coronary stent in patients presenting with ST-segment elevation myocardial infarction: results from the APPOSITION III registry.**

Koch KT1, Grundeken MJ, Vos NS, **IJsselmuiden AJ**, van Geuns RJ, Wessely R, Dengler T, La Manna A, Silvain J, Montalescot G, Spaargaren R, Tijssen JG, Amoroso G. EuroIntervention. 2015 Jul 22;11(3):264-71. doi: 10.4244/EIJY15M02\_08.

AIMS: The aim of APPOSITION III was to evaluate the feasibility and performance of the STENTYS Self-Apposing<sup>®</sup> stent (STENTYS S.A., Paris, France) in the setting of primary percutaneous coronary intervention (PCI).

METHODS AND RESULTS: APPOSITION III was an international, prospective, multicentre registry. The study population consisted of 965 patients. The rate of the primary endpoint major adverse cardiac events (MACE), defined as the composite of cardiac death, recurrent target vessel myocardial infarction (TV-MI), and clinically driven target lesion revascularisation (CD-TLR), at one year was 9.3%. One-year cardiac death rate was 2.0%, TV-MI rate was 1.3%, CD-TLR rate was 7.4% and definite/probable stent thrombosis (ST) rate was 3.5% (definite ST 2.8%). An interim safety analysis of in-hospital outcomes in the first 400 patients showed higher event rates if post-dilation was not performed, and post-dilations became highly recommended in the remaining cohort. Patients undergoing post-dilation eventually showed a numerically lower one-year MACE rate (8.4% vs. 11.3%,  $p=0.137$ ). One-year TV-MI (0.8% vs. 2.5%,  $p=0.027$ ) and definite ST (1.9% vs. 5.0%,  $p=0.010$ ) rates were significantly lower if post-dilation was performed, with the divergence occurring at <30 days.

CONCLUSIONS: The use of the STENTYS Self-Apposing<sup>®</sup> stent in the setting of primary PCI was feasible and associated with acceptable cardiovascular event rates which improved when post-dilation was performed.

PMID: 25692610

**Repetitive stress-induced cardiomyopathy due to inverted Takotsubo in exaggerated sympathetic stimulation by pheochromocytoma.**

Brugts JJ1, **van Gent M2**, Caliskan K3, **Kofflard MJ2**.

Eur Heart J Cardiovasc Imaging. 2015 Jan;16(1):113. doi: 10.1093/ehjci/jeu159. Epub 2014 Sep 3.

PMID: 25187605

**Revealing the impact of local access-site complications and upper extremity dysfunction post transradial percutaneous coronary procedures.**

**Zwaan EM1, Koopman AG1, Holtzer CA2, Zijlstra F3, Ritt MJ4, Amoroso G5, Moerman E6, Kofflard MJ1, IJsselmuiden AA7.**

Neth Heart J. 2015 Nov;23(11):514-24. doi: 10.1007/s12471-015-0747-9.

**OBJECTIVES:** Little is known about local access-site complications and upper extremity dysfunction after transradial percutaneous coronary procedures (TR-PCP). This systematic review study aimed to summarise the current knowledge on the incidences of access-site complications and upper extremity dysfunction after TR-PCP.

**METHODS:** Two independent, trained investigators searched MEDLINE, EMBASE and CENTRAL for eligible studies published before 1 January 2015. Also, they hand-searched the conference proceedings of the annual scientific sessions of the American College of Cardiology, the American Heart Association, European Society of Cardiology, and the Trans-catheter Cardiovascular Therapeutics. Inclusion criteria were cohort studies and clinical trials discussing the incidence of access-site complications and upper extremity function after transradial percutaneous coronary intervention (TR-PCI) and/or transradial coronary angiography (TR-CAG) as endpoints.

**RESULTS:** 176 articles described access-site complications. The incidence is up to 9.6%. Fourteen articles described upper extremity dysfunction, with an incidence of up to 1.7%. Upper extremity dysfunction was rarely investigated, hardly ever as primary endpoint, and if investigated not thoroughly enough.

**CONCLUSION:** Upper extremity dysfunction in TR-PCP has never been properly investigated and is therefore underestimated. Further studies are needed to investigate the magnitude, prevention and best treatment of upper extremity dysfunction. Optimising TR-PCP might be achieved by using slender techniques, detection of upper extremity dysfunction and early referral to a hand rehabilitation centre.

**KEYWORDS:** Access-site complication; Radial artery; Upper extremity dysfunction

PMID: 26437970

## Case report of a proximal humeral fracture with an avulsion fracture of the lesser tuberosity in an adolescent girl.

**Koper MC1, Jakma TS2.**

J Shoulder Elbow Surg. 2015 Sep;24(9):e260-3. doi: 10.1016/j.jse.2015.05.054. Epub 2015 Jul 15.

Fractures of the proximal humerus in the adolescent population are rare and account for about 4% of all fractures. This number is increasing, especially because adolescents place higher demands on their shoulder joints as a result of high levels of activity.<sup>5</sup> Nonsurgical treatment for proximal humeral fractures in adolescents is widely accepted. Multiple studies show good to excellent clinical results. About 80% of the longitudinal growth of the humerus comes from the proximal humeral physis, which favors the nonsurgical treatment.

PMID: 26187137

## Classification of proximal tibial epiphysis fractures in children: Four clinical cases.

**Aerts BR1, Ten Brinke B2, Jakma TS2, Punt BJ2.**

Injury. 2015 Aug;46(8):1680-3. doi: 10.1016/j.injury.2015.05.039. Epub 2015 May 27.

PMID: 26100208

## Effect of a ward-based pharmacy team on preventable adverse drug events in surgical patients (SUREPILL study).

Surgery and Pharmacy in Liaison (SUREPILL) Study Group.

Collaborators: de Boer M, Boeker EB, Ramrattan MA, Kiewiet JJ, Ram K, Gombert-Handoko KB, van Lent-Evers NA, Kuks PF, Mulder WM, Breslau PJ, **Oostenbroek RJ**, Dijkgraaf MG, Lie-A-Huen L, Boermeester MA.

Br J Surg. 2015 Sep;102(10):1204-12. doi: 10.1002/bjs.9876. Epub 2015 Jul 14.

**BACKGROUND:** Surgical patients are at risk of adverse drug events (ADEs) causing morbidity and mortality. Much harm is preventable. Ward-based pharmacy interventions to reduce medication-related harm have not been evaluated in surgical patients.

**METHODS:** This multicentre prospective clinical trial evaluated a protocolled, ward-based pharmacy method compared with standard pharmaceutical care in surgical patients. Allocation of study group was done by one-time randomization at ward level. Consecutive patients admitted for elective surgery with an expected hospital stay longer than 48 h were included. Pharmacy practitioners performed bedside medication reconciliation at admission and discharge, and hospital pharmacists undertook regular medication reviews in the study wards. Preventable ADEs and clinical outcomes were assessed.

**RESULTS:** A total of 1094 surgical patients were studied. Some 880 specific interventions were made by the hospital pharmacist to improve pharmacotherapy in 309 of 547 patients on study

wards. A further 547 patients were included on control wards. A crude non-significant reduction in incidence of preventable ADEs was seen on intervention wards in comparison with control wards (2.74 versus 3.84 preventable ADEs per 100 admissions; incidence rate ratio 0.71, 95 per cent c.i. 0.37 to 1.39;  $P = 0.324$ ). After adjustment for differences in treatment groups and for potential confounding, the incidence rate ratio remained non-significant (0.82, 0.39 to 1.72;  $P = 0.598$ ). No differences were seen for other outcomes, such as duration of hospital stay, number of complications and quality of life.

**CONCLUSION:** The present prospective controlled trial showed no significant reduction in medication-related harm or changes in clinical outcomes when surgical patients received protocolled ward-based pharmacy interventions.

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PMID: 26179814

### **Factors affecting timing of closure and non-reversal of temporary ileostomies.**

**Sier MF1, van Gelder L, Ubbink DT, Bemelman WA, Oostenbroek RJ.**

Int J Colorectal Dis. 2015 Sep;30(9):1185-92. doi: 10.1007/s00384-015-2253-3.

Epub 2015 Jun 9.

**BACKGROUND:** Although stoma closure is considered a simple surgical intervention, the interval between construction and reversal is often prolonged, and some ileostomies may never be reversed. We evaluated possible predictors for non-reversal and prolonged interval between construction and reversal.

**MATERIAL AND METHODS:** In a cohort study of ileostomy patients treated in a large teaching hospital, we collected data from the surgical complication and enterostomal therapists' registries between January 2001 and December 2011. Parameters responsible for morbidity, mortality, length of stay and time interval between construction and reversal were analysed.

**RESULTS:** Of 485 intentionally temporary ileostomies, 359 were reversed after a median of 5.6 months (IQR 3.8-8.9 months), while 126 (26 %) remained permanent. End ileostomy and intra-abdominal abscess independently delayed reversal. Age, end ileostomy, higher body mass index and preoperative radiotherapy were independent factors for non-reversal.

Median duration of hospitalisation for reversal was 7.0 days (5-13 days). Morbidity and mortality were 31 and 0.9 %, respectively. In 20 patients (5.5 %), re-ileostomy was necessary.

**CONCLUSIONS:** A substantial number of ileostomies that are intended to be temporary will never be reversed. If reversed, the interval between construction and reversal is longer than anticipated, while morbidity after reversal and duration of hospitalisation are considerable.

Besides a temporary ileostomy, there are two other options: no diversion or a permanent colostomy. Shared decision-making is to be preferred in these situations.

PMID: 26054385

### **Intensified follow-up in colorectal cancer patients using frequent Carcino-Embryonic Antigen (CEA) measurements and CEA-triggered imaging: Results of the randomized "CEAwatch" trial.**

Verberne CJ1, Zhan Z2, van den Heuvel E3, Grossmann I4, Doornbos PM5, Havenga K6, Manusama E7, Klaase J8, van der Mijle HC9, **Lamme B10**, Bosscha K11, Baas P12, van Ooijen B13, Nieuwenhuijzen G14, Marinelli A15, van der Zaag E16, Wasowicz D17, de Bock GH18, Wiggers T19.

Eur J Surg Oncol. 2015 Sep;41(9):1188-96. doi: 10.1016/j.ejso.2015.06.008. Epub 2015 Jun 30.

**AIM:** The value of frequent Carcino-Embryonic Antigen (CEA) measurements and CEA-triggered imaging for detecting recurrent disease in colorectal cancer (CRC) patients was investigated in search for an evidence-based follow-up protocol.

**METHODS:** This is a randomized-controlled multicenter prospective study using a stepped-wedge cluster design. From October 2010 to October 2012, surgically treated non-metastatic CRC patients in follow-up were followed in eleven hospitals. Clusters of hospitals sequentially changed their usual follow-up care into an intensified follow-up schedule consisting of CEA measurements every two months, with imaging in case of two CEA rises. The primary outcome measures were the proportion of recurrences that could be treated with curative intent, recurrences with definitive curative treatment outcome, and the time to detection of recurrent disease.

**RESULTS:** 3223 patients were included; 243 recurrences were detected (7.5%). A higher proportion of recurrences was detected in the intervention protocol compared to the control protocol (OR = 1.80; 95%-CI: 1.33-2.50; p = 0.0004). The proportion of recurrences that could be treated with curative intent was higher in the intervention protocol (OR = 2.84; 95%-CI: 1.38-5.86; p = 0.0048) and the proportion of recurrences with definitive curative treatment outcome was also higher (OR = 3.12, 95%-CI: 1.25-6.02, p-value: 0.0145). The time to detection of recurrent disease was significantly shorter in the intensified follow-up protocol (HR = 1.45; 95%-CI: 1.08-1.95; p = 0.013).

**CONCLUSION:** The CEAwatch protocol detects recurrent disease after colorectal cancer earlier, in a phase that a significantly higher proportion of recurrences can be treated with curative intent.

**KEYWORDS:** CEA; Colorectal cancer; Follow-up; Stepped-wedge cluster randomized trial (SW-RCT)

PMID: 26184850

### Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial.

Vennix S, Musters GD, Mulder IM, Swank HA, Consten EC, Belgers EH, van Geloven AA, Gerhards MF, Govaert MJ, van Grevenstein WM, Hoofwijk AG, Kruijt PM, Nienhuijs SW, Boermeester MA, Vermeulen J, van Dieren S, Lange JF, Bemelman WA; Ladies trial collaborators. Collaborators: ... **van der Hoeven JA**, ... **Plaisier PW** ...

Lancet. 2015 Sep 26;386(10000):1269-77. doi: 10.1016/S0140-6736(15)61168-0. Epub 2015 Jul 22.

Comment in: Laparoscopic peritoneal lavage for perforated diverticulitis: in search of evidence. [Lancet. 2015]

**BACKGROUND:** Case series suggest that laparoscopic peritoneal lavage might be a promising alternative to sigmoidectomy in patients with perforated diverticulitis. We aimed to assess the superiority of laparoscopic lavage compared with sigmoidectomy in patients with purulent perforated diverticulitis, with respect to overall long-term morbidity and mortality.

**METHODS:** We did a multicentre, parallel-group, randomised, open-label trial in 34 teaching hospitals and eight academic hospitals in Belgium, Italy, and the Netherlands (the Ladies trial). The Ladies trial is split into two groups: the LOLA group comparing laparoscopic lavage with sigmoidectomy and the DIVA group comparing Hartmann's procedure with sigmoidectomy

plus primary anastomosis. The DIVA section of this trial is still underway but here we report the results of the LOLA section. Patients with purulent perforated diverticulitis were enrolled for LOLA, excluding patients with faecal peritonitis, aged older than 85 years, with high-dose steroid use ( $\geq 20$  mg daily), and haemodynamic instability. Patients were randomly assigned (2:1:1; stratified by age [ $< 60$  years vs  $\geq 60$  years]) using secure online computer randomisation to laparoscopic lavage, Hartmann's procedure, or primary anastomosis in a parallel design after diagnostic laparoscopy. Patients were analysed according to a modified intention-to-treat principle and were followed up after the index operation at least once in the outpatient setting and after sigmoidoscopy and stoma reversal, according to local protocols. The primary endpoint was a composite endpoint of major morbidity and mortality within 12 months. This trial is registered with ClinicalTrials.gov, number NCT01317485.

**FINDINGS:** Between July 1, 2010, and Feb 22, 2013, 90 patients were randomly assigned in the LOLA section of the Ladies trial when the study was terminated by the data and safety monitoring board because of an increased event rate in the lavage group. Two patients were excluded for protocol violations. The primary endpoint occurred in 30 (67%) of 45 patients in the lavage group and 25 (60%) of 42 patients in the sigmoidectomy group (odds ratio 1.28, 95% CI 0.54-3.03,  $p=0.58$ ). By 12 months, four patients had died after lavage and six patients had died after sigmoidectomy ( $p=0.43$ ).

**INTERPRETATION:** Laparoscopic lavage is not superior to sigmoidectomy for the treatment of purulent perforated diverticulitis.

**FUNDING:** Netherlands Organisation for Health Research and Development. Copyright © 2015 Elsevier Ltd. All rights reserved.

PMID: 26209030

### Performance indicators for lung cancer surgery in the Netherlands

Damhuis RA1, Maat AP2, **Plaisier PW3**

Eur J Cardiothorac Surg. 2015 May;47(5):897-903; discussion 903-4. doi: 10.1093/ejcts/ezu329. Epub 2014 Sep 3.

**OBJECTIVES:** In the Netherlands, surgery for lung cancer is traditionally performed in low-volume hospitals. To assess the need for centralization, we examined early outcome measures and compared results between hospitals and with other European countries.

**METHODS:** Data on patient, tumour and treatment characteristics were retrieved from the Netherlands Cancer Registry. Results were tabulated for 30-day postoperative mortality (POM), major morbidity rate (intrathoracic empyema, bronchopleural fistula or rethoracotomy) and pneumonectomy proportion. Hospital variation was projected using funnel graphs in which the results for individual hospitals are plotted against volume.

**RESULTS:** The study comprised a series of 9579 patients with primary non-small cell lung cancer, diagnosed from 2005 through 2010 and operated in 79 different hospitals. The POM was 2.7% on average and age, gender, period and type of surgery were determined as prognostic factors. Multivariable analysis did not reveal an association with hospital volume ( $P = 0.34$ ). The POM was higher for operations on Fridays (4.0%) or during weekends (6.8%). Major morbidity was observed after 8.3% of operations and was more frequent after bilobectomy (11.6%) or right pneumonectomy (22%). The pneumonectomy proportion decreased from 18% in 2005 to 11% in 2010. Funnel plots revealed a limited number of significant outliers, despite combining data over a 6-year period.

**CONCLUSIONS:** Results for the Netherlands were similar to those from other European

countries. Hospital volume was not associated with early outcome indicators. Quality assessment at the hospital level remains a major challenge given the low frequency of adverse events and the impediments of chance variation.

KEYWORDS: Hospital volume; Lung cancer; Pneumonectomy; Postoperative mortality; Quality indicators

PMID: 25187534

### **Magnetic Resonance Imaging in Patients with Unilateral Bloody Nipple Discharge; Useful When Conventional Diagnostics are Negative?**

**van Gelder L1, Bisschops RH, Menke-Pluymers MB, Westenend PJ, Plaisier PW.**

World J Surg. 2015 Jan;39(1):184-6. doi: 10.1007/s00268-014-2701-1.

BACKGROUND: Unilateral bloody nipple discharge (UBND) is mostly caused by benign conditions such as papilloma or ductal ectasia. However, in 7-33 % of all nipple discharge, it is caused by breast cancer. Conventional diagnostic imaging like mammography (MMG) and ultrasonography (US) is performed to exclude malignancy. Preliminary investigations of breast magnetic resonance imaging (MRI) assume that it has additional value. With an increasing availability of MRI, it is of clinical importance to evaluate this. We evaluated the additional diagnostic value of MRI in patients with UBND in the absence of a palpable mass, with normal conventional imaging.

METHODS: All women with UBND in the period November 2007-July 2012 were included. In addition to the standard work-up (patient's history, physical examination, MMG, and US), MRI was performed. Data from these examinations and treatment were collected retrospectively.

RESULTS: A total of 111 women (mean age 52 years; range 23-80) were included. In nine (8 %) patients, malignancy was suspected on MRI while conventional imaging was normal. In eight (89 %) of these patients, histology was obtained, two by core biopsy and six by terminal duct excision. Benign conditions were found in six patients (86 %) and a (pre-) malignant lesion in two patients. In both cases, it concerned a ductal carcinoma in situ, which was treated with breast-conserving therapy. Moreover, in two cases of (pre)malignancy, the MRI was interpreted as negative.

CONCLUSION: In patients with UBND who show no signs of a malignancy on conventional diagnostic examinations, the added value of a breast MRI is limited, since a malignancy can be demonstrated in <2 %.

PMID: 25123174

### **Multiparametric MRI With Dynamic Contrast Enhancement, Diffusion-Weighted Imaging, and 31-Phosphorus Spectroscopy at 7 T for Characterization of Breast Cancer.**

Schmitz AM1, Veldhuis WB, **Menke-Pluijmers MB**, van der Kemp WJ, van der Velden TA, **Kock MC, Westenend PJ**, Klomp DW, Gilhuijs KG.

Invest Radiol. 2015 Nov;50(11):766-71. doi: 10.1097/RLI.0000000000000183.

OBJECTIVES: To describe and to correlate tumor characteristics on multiparametric 7 tesla (T) breast magnetic resonance imaging (MRI) with prognostic characteristics from postoperative histopathology in patients with breast cancer.

MATERIALS AND METHODS: Institutional review board approval and written informed consent

of 15 women (46-70 years) with 17 malignant lesions were obtained. In this prospective study (March 2013 to March 2014), women were preoperatively scanned using dynamic contrast-enhanced MRI, diffusion-weighted imaging, and 31-phosphorus spectroscopy (P-MRS). The value of the protocol was assessed to quantify tumor differentiation and proliferation. Dynamic contrast-enhanced MRI was assessed according to the American College of Radiology Breast Imaging Reporting and Data System-MRI lexicon. Apparent diffusion coefficients (ADCs) were calculated from diffusion-weighted imaging. On P-MRS, at the location of the tumor, the amount of phosphorus components was obtained in a localized spectrum. In this spectrum, the height of phosphodiester (PDE) and phosphomonoester (PME) peaks was assessed to serve as a measure for metabolic activity, stratifying tumors into a PDE > PME, PDE = PME, or PDE < PME group. Tumor grade and mitotic count from resection specimen were compared with the MRI characteristics using explorative analyses.

**RESULTS:** On dynamic contrast-enhanced MRI, the mean tumor size was 24 mm (range, 6-55 mm). An inverse trend was seen between ADC and tumor grade ( $P = 0.083$ ), with mean ADC of  $867 \times 10 \text{ mm}^2/\text{s}$  for grade 1 ( $N = 4$ ),  $751 \times 10 \text{ mm}^2/\text{s}$  for grade 2 ( $N = 6$ ), and  $659 \times 10 \text{ mm}^2/\text{s}$  for grade 3 ( $N = 2$ ) tumors. Between P-MR spectra and mitotic count, a relative increase of PME over PDE showed significant association with increasing mitotic counts ( $P = 0.02$ ); a mean mitotic count of 6 was found in the PDE greater than PME group ( $N = 7$ ), 8 in the PDE = PME group ( $N = 1$ ), and 17 in the PDE < PME group ( $N = 3$ ).

**CONCLUSIONS:** Multiparametric 7 T breast MRI is feasible in clinical setting and shows association between ADC and tumor grade, and between P-MRS and mitotic count.

PMID: 26135017

### Prophylactic mesh placement to prevent parastomal hernia, early results of a prospective multicentre randomized trial.

Brandsma HT1, Hansson BM2, Aufenacker TJ3, van Geldere D4, van Lammeren FM5, Mahabier C6, Steenvoorde P7, de Vries Reilingh TS8, Wiezer RJ9, de Wilt JH10, Bleichrodt RP2, Rosman C2.

Hernia. 2015 Oct 28. [Epub ahead of print]

**PURPOSE:** Parastomal hernia (PSH) is a common complication after colostomy formation. Recent studies indicate that mesh implantation during formation of a colostomy might prevent a PSH. To determine if placement of a retromuscular mesh at the colostomy site is a feasible, safe and effective procedure in preventing a parastomal hernia, we performed a multicentre randomized controlled trial in 11 large teaching hospitals and three university centres in The Netherlands.

**METHODS:** Augmentation of the abdominal wall with a retromuscular light-weight polypropylene mesh (Parietene Light™, Covidien) around the trephine was compared with traditional colostomy formation. Patients undergoing elective open formation of a permanent end-colostomy were eligible. 150 patients were randomized between 2010 and 2012. Primary endpoint of the PREVENT trial is the incidence of parastomal hernia. Secondary endpoints are morbidity, pain, quality of life, mortality and cost-effectiveness. This article focussed on the early results of the PREVENT trial and, therefore, operation time, postoperative morbidity, pain, and quality of life were measured.

**RESULTS:** Outcomes represent results after 3 months of follow-up. A total of 150 patients were randomized. Mean operation time of the mesh group ( $N = 72$ ) was significantly longer than in the control group ( $N = 78$ ) (182.6 vs. 156.8 min;  $P = 0.018$ ). Four (2.7 %) peristomal

infections occurred of which one (1.4 %) in the mesh group. No infection of the mesh occurred. Most of the other infections were infections of the perineal wound, equally distributed over both groups. No statistical differences were discovered in stoma or mesh-related complications, fistula or stricture formation, pain, or quality of life. **CONCLUSIONS:** During open and elective formation of an end-colostomy, primary placement of a retromuscular light-weight polypropylene mesh for prevention of a parastomal hernia is a safe and feasible procedure. The PREVENT trial is registered at: <http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=2018>. **KEYWORDS:** Colostomy; Hernia; Mesh; Parastomal hernia; Prevention

PMID: 26511879

### Spontaneous sternal fracture due to multiple myeloma requiring extensive surgical repair.

**Reuling EM1, Jakma TS1, Schnater JM1, Westerweel PE2.**

BMJ Case Rep. 2015 Nov 30;2015. pii: bcr2015211498. doi: 10.1136/bcr-2015-211498.

Spontaneous sternal fracture is a well-known complication of multiple myeloma due to osteolytic bone lesions. The possibility of a multiple myeloma should be thoroughly investigated in patients presenting with a spontaneous sternal fracture. This work up should go beyond protein electrophoresis alone as a monoclonal paraprotein is not always present. In some cases, the myeloma plasma cell clone produces only the free light chain ( or ) or may even be non-secretory. The underlying plasma cell dyscrasia is treated with chemotherapy and, if needed, local radiotherapy. However, for patients with a fracture causing persistent pain and physical discomfort, internal fixation may be additionally required. We present a case of a patient who presented with a displaced pathological sternal fracture. She was treated with chemotherapy, radiotherapy and an open reduction and internal fixation with a Locking Compression Plate (LCP). This technique offers a feasible option for rigid fixation of pathological fractures.

PMID: 26621901

### Using a gene expression signature when controversy exists regarding the indication for adjuvant systemic treatment reduces the proportion of patients receiving adjuvant chemotherapy: a nationwide study.

Kuijjer A1, van Bommel AC2, **Drukker CA3**, van der Heiden-van der Loo M4, Smorenburg CH5, **Westenend PJ6**, Linn SC5, Rutgers EJ7, Elias SG8, van Dalen T1.

Genet Med. 2015 Nov 19. doi: 10.1038/gim.2015.152. [Epub ahead of print]

**PURPOSE:** The Dutch national guideline advises use of gene-expression signatures, such as the 70-gene signature (70-GS), in case of ambivalence regarding the benefit of adjuvant chemotherapy (CT). In this nationwide study, the impact of 70-GS use on the administration of CT in early breast cancer patients with a dubious indication for CT is assessed.

**METHODS:** Patients within a national guideline directed indication area for 70-GS use who were surgically treated between November 2011 and April 2013 were selected from the Netherlands Cancer Registry database. The effect of 70-GS use on the administration of CT was evaluated in guideline- and age-delineated subgroups addressing potential effect of bias by linear mixed-effect modeling and instrumental variable (IV) analyses.

**RESULTS:** A total of 2,043 patients within the indicated area for 70-GS use were included,

of whom 298 received a 70-GS. Without use of the 70-GS, 45% of patients received CT. The 70-GS use was associated with a 9.5% decrease in CT administration (95% confidence interval (CI): -15.7 to -3.3%) in linear mixed-effect model analyses and IV analyses showed similar results (-9.9%; 95% CI: -19.3 to -0.4).

CONCLUSION: In patients in whom the Dutch national guidelines suggest the use of a gene-expression profile, 70-GS use is associated with a 10% decrease in the administration of adjuvant CT. *Genet Med* advance online publication 19 November 2015 *Genetics in Medicine* (2015);

PMID: 26583684

### Validity and Reliability of Global Operative Assessment of Laparoscopic Skills (GOALS) in Novice Trainees Performing a Laparoscopic Cholecystectomy.

Kramp KH1, van Det MJ2, Hoff C3, Lamme B4, Veeger NJ5, Pierie JP6.

*J Surg Educ.* 2015 Mar-Apr;72(2):351-8. doi: 10.1016/j.jsurg.2014.08.006. Epub 2014 Oct 16.

PURPOSE: Global Operative Assessment of Laparoscopic Skills (GOALS) assessment has been designed to evaluate skills in laparoscopic surgery. A longitudinal blinded study of randomized video fragments was conducted to estimate the validity and reliability of GOALS in novice trainees.

METHODS: In total, 10 trainees each performed 6 consecutive laparoscopic cholecystectomies. Sixty procedures were recorded on video. Video fragments of (1) opening of the peritoneum; (2) dissection of Calot's triangle and achievement of critical view of safety; and (3) dissection of the gallbladder from the liver bed were blinded, randomized, and rated by 2 consultant surgeons using GOALS. Also, a grade was given for overall competence. The correlation of GOALS with live observation Objective Structured Assessment of Technical Skills (OSATS) scores was calculated. Construct validity was estimated using the Friedman 2-way analysis of variance by ranks and the Wilcoxon signed-rank test. The interrater reliability was calculated using the absolute and consistency agreement 2-way random-effects model intraclass correlation coefficient.

RESULTS: A high correlation was found between mean GOALS score ( $r = 0.879$ ,  $p = 0.021$ ) and mean OSATS score. The GOALS score increased significantly across the 6 procedures ( $p = 0.002$ ). The trainees performed significantly better on their sixth when compared with their first cholecystectomy ( $p = 0.004$ ). The consistency agreement interrater reliability was 0.37 for the mean GOALS score ( $p = 0.002$ ) and 0.55 for overall competence ( $p < 0.001$ ) of the 3 video fragments.

CONCLUSION: The validity observed in this randomized blinded longitudinal study supports the existing evidence that GOALS is a valid tool for assessment of novice trainees. A relatively low reliability was found in this study.

KEYWORDS: Interpersonal and Communication Skills; Practice-Based Learning and Improvement; Systems-Based Practice; assessment; laparoscopic cholecystectomy; laparoscopy; trainee; videotape recording

PMID: 25441259

## Why Patencies of Femoropopliteal Bypass Grafts with Distal End-to-End Anastomosis are Comparable with End-to-Side Anastomosis.

Hoedt M1, How T, Poyck P, Wittens C.

Ann Thorac Cardiovasc Surg. 2015;21(2):157-64. doi: 10.5761/atcs.oa.14-00121.

Epub 2015 Jan 26.

Objective: Despite the theoretical favourable hemodynamic advantage of end-to-end anastomosis (ETE), femoropopliteal bypasses with distal ETE and end-to-side anastomosis (ETS) have comparable clinical patencies. We therefore studied the effects of different in vivo anastomotic configurations on hemodynamics in geometrically realistic ETE and ETS in vitro flow models to explain this phenomenon.

Methods: Four ETE and two ETS models (30° and 60°) were constructed from in vivo Computed Tomography Angiography data. With flow visualization physiological flow conditions were studied. Results: In ETS, a flow separation and recirculation zone was apparent at anastomotic edges with a shifting stagnation point between them during systole. Secondary flow patterns developed with flow deceleration and reversal. Slight out of axis geometry of all ETE resulted in flow separation and recirculation areas comparable to ETS. Vortical flow patterns were more stable in wider and longer bevelled ETE. Conclusion: Primary flow disturbances in ETE are comparable to ETS and are related to the typical sites where myointimal hyperplasia develops. In ETS, reduction of anastomosis angle will diminish flow disturbances. To reduce flow disturbances in ETE, the creation of a bulbous spatulation with resulting axial displacement of graft in relation to recipient artery should be prevented.

PMID: 25641036

# Dermatologie

## **A 7-year-old boy with fever, rash and coughing. Erythema multiforme (EM) major.**

**van der Bent SA1, van Ham-Borawitz VE, de Kleijn ED, Reeder SW, Laeijendecker R.**  
Neth J Med. 2015 Jul;73(6):302-3.

PMID: 26228199

## **[A boy with a chronic swelling of the upper lip].**

**van der Bent SA1, Kuizinga MC, van der Velden JJ.**

Ned Tijdschr Geneeskd. 2015;159(0):A9103.

A 14-year-old boy developed a chronic painless swelling of the upper lip. Histology of a skin biopsy showed non-necrotizing tuberculoid granulomas. The diagnosis cheilitis granulomatosa was made.

PMID: PMID: 26230346 [PubMed - in process]

## **Induction therapy with a combination of fumarates and cyclosporine: A benefit for the patient?**

**Fallah Arani S1,2, Neumann HA2, Thio HB2.**

J Dermatolog Treat. 2015 Dec 10:1-2. [Epub ahead of print]

Fumarates or fumaric acid esters derivatives (FAED) have appeared to be effective and less toxic than other systemic treatments for psoriasis. Due to its safe adverse event profile, FAED can be used as a long-term maintenance therapy. One of the greatest reasons why FAED are not preferred as a first-line treatment is that according to the recommended dosing schedule, clinically meaningful improvement is seen just after 6 to 8 weeks of therapy. In this manuscript, we suppose an alternative induction scheme with a combination therapy of fumarates and cyclosporine for a more rapid improvement and better compliance.

KEYWORDS: Fumarates; combination; cyclosporine; fumaric acid esters derivatives; psoriasis; therapy; treatment

PMID: 26651839

# Gynaecologie

## **Behavioural and neurodevelopmental outcome of 2-year-old children after preterm premature rupture of membranes: follow-up of a randomised clinical trial comparing induction of labour and expectant management.**

van der Heyden JL1, Willekes C2, van Baar AL3, van Wassenaer-Leemhuis AG4, Pajkrt E4, Oudijk MA5, Porath MM6, Duvekot HJ7, Bloemenkamp KW8, Groenewout M9, Woiski M10, Nij Bijvank B11, Bax CJ12, van 't Hooft J4, Sikkema MJ13, **Akerboom BM14**, Mulder TA2, Nijhuis JG2, Mol BW15, van der Ham DP16.

Eur J Obstet Gynecol Reprod Biol. 2015 Aug 3;194:17-23. doi: 10.1016/j.ejogrb.2015.07.014. [Epub ahead of print]

**OBJECTIVE:** We recently reported that induction of labour does not improve short term neonatal outcome in women with late preterm premature rupture of membranes (PPROM) as compared to expectant management (PPROMEXIL trial). In this study the neurodevelopmental and behavioural outcome of the children from this trial at 2 years of age was studied.

**STUDY DESIGN:** We studied outcome of offspring of women randomised in the PPROMEXIL study. These women had >24h of ruptured membranes and were between 34 and 37 weeks of pregnancy when they were randomised to induction of labour (IoL) or expectant management (EM). Two years after delivery, the parents received the ages and stages questionnaire (ASQ), the child behaviour checklist (CBCL) and a general questionnaire. **RESULTS:** Follow-up data were obtained from 234 children (121 after IoL, 113 after EM, response rate 59% (44% of the original 532 randomised women)). In the IoL group 16 children (14%) had an abnormal score in  $\geq 1$  domains of the ASQ, versus 27 (26%) in the EM group (difference in percentage -11.4 (95% CI -21.9 to -0.98;  $p=0.033$ )). For the CBCL, an abnormal score was found in 13% ( $n=15$ ) in the IoL group and in 15% ( $n=16$ ) in the EM group (difference in percentage -2.13 (95% CI -11.2 to 6.94;  $p=0.645$ )).

**CONCLUSION:** Although a policy of induction of labour in women with late PPROM does not improve short term neonatal outcome, it might be associated with a decrease in neurodevelopmental difficulties at the age of two years as compared to expectant management. Expectant management did not lead to a difference in behavioural problems.

PMID: 26319651

## **Effect of levothyroxine on live birth rate in euthyroid women with recurrent miscarriage and TPO antibodies (T4-LIFE study).**

Vissenberg R1, van Dijk MM2, Fliers E3, van der Post JA4, van Wely M2, Bloemenkamp KW5, Hoek A6, Kuchenbecker WK7, H R Verhoeve8, H C J Scheepers9, **Rombout-de Weerd S10**, Koks C11, Zwart JJ12, Broekmans F13, Verpoest W14, Christiansen O15, M Post16, Papatsonis DN17, Verberg MF18, Sikkema J19, Mol BW20, Bisschop PH3, Goddijn M2.

Contemp Clin Trials. 2015 Aug 5. pii: S1551-7144(15)30061-6. doi: 10.1016/j.cct.2015.08.005. [Epub ahead of print]

**BACKGROUND:** Thyroid peroxidase antibodies (TPO-Ab) in euthyroid women are associated with recurrent miscarriage (RM) and other pregnancy complications such as preterm birth.

It is unclear if treatment with levothyroxine improves pregnancy outcome. Aim To determine the effect of levothyroxine administration on live birth rate in euthyroid TPO-Ab positive women with recurrent miscarriage.

**METHODS:** /Design We will perform a multicenter, placebo controlled randomized trial in euthyroid women with recurrent miscarriage and TPO-Ab. Recurrent miscarriage is defined as two or more miscarriages before the 20th week of gestation. The primary outcome is live birth, defined as the birth of a living fetus beyond 24weeks of gestation. Secondary outcomes are ongoing pregnancy at 12weeks, miscarriage, preterm birth, (serious) adverse events, time to pregnancy and survival at 28days of neonatal life. The analysis will be performed according to the intention to treat principle. We need to randomize 240 women (120 per group) to demonstrate an improvement in live birth rate from 55% in the placebo group to 75% in the levothyroxine treatment group. This trial is a registered trial (NTR 3364, March 2012). Here we discuss the rationale and design of the T4-LIFE study, an international multi-center randomized, double blind placebo controlled, clinical trial aimed to assess the effectiveness of levothyroxine in women with recurrent miscarriage and TPO-Ab.

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**KEYWORDS:** Recurrent miscarriage; TPO antibodies; levothyroxine; live birth rate; preterm birth; thyroid autoimmunity

PMID: 26255238

### Is IVF-served two different ways-more cost-effective than IUI with controlled ovarian hyperstimulation?

Tjon-Kon-Fat R11, Bendsdorp AJ1, Bossuyt PM2, Koks C3, Oosterhuis GJ4, Hoek A5, Hompes P6, Broekmans FJ7, Verhoeve HR8, de Bruin JP9, van Golde R10, Repping S1, Cohlen BJ11, **Lambers MD12**, van Bommel PF13, Slappendel E14, Perquin D15, Smeenk J16, Pelinck MJ17, Gianotten J18, Hoozemans DA19, Maas JW3, Groen H5, Eijkemans MJ20, van der Veen F1, Mol BW21, van Wely M22.

Hum Reprod. 2015 Oct;30(10):2331-9. doi: 10.1093/humrep/dev193. Epub 2015 Aug 12.

**STUDY QUESTION:** What is the cost-effectiveness of in vitro fertilization (IVF) with conventional ovarian stimulation, single embryo transfer (SET) and subsequent cryocycles or IVF in a modified natural cycle (MNC) compared with intrauterine insemination with controlled ovarian hyperstimulation (IUI-COH) as a first-line treatment in couples with unexplained subfertility and an unfavourable prognosis on natural conception?.

**SUMMARY ANSWER:** Both IVF strategies are significantly more expensive when compared with IUI-COH, without being significantly more effective. In the comparison between IVF-MNC and IUI-COH, the latter is the dominant strategy. Whether IVF-SET is cost-effective depends on society's willingness to pay for an additional healthy child.

**WHAT IS KNOWN ALREADY:** IUI-COH and IVF, either after conventional ovarian stimulation or in a MNC, are used as first-line treatments for couples with unexplained or mild male subfertility. As IUI-COH is less invasive, this treatment is usually offered before proceeding to IVF. Yet, as conventional IVF with SET may lead to higher pregnancy rates in fewer cycles for a lower multiple pregnancy rate, some have argued to start with IVF instead of IUI-COH. In addition, IVF in the MNC is considered to be a more patient friendly and less costly form of IVF.

**STUDY DESIGN, SIZE, DURATION:** We performed a cost-effectiveness analysis alongside a randomized noninferiority trial. Between January 2009 and February 2012, 602 couples with unexplained infertility and a poor prognosis on natural conception were allocated to three cycles of IVF-SET including frozen embryo transfers, six cycles of IVF-MNC or six cycles of

IUI-COH. These couples were followed until 12 months after randomization.

**PARTICIPANTS/MATERIALS, SETTING, METHODS:** We collected data on resource use related to treatment, medication and pregnancy from the case report forms. We calculated unit costs from various sources. For each of the three strategies, we calculated the mean costs and effectiveness. Incremental cost-effectiveness ratios (ICER) were calculated for IVF-SET compared with IUI-COH and for IVF-MNC compared with IUI-COH. Nonparametric bootstrap resampling was used to investigate the effect of uncertainty in our estimates. **MAIN RESULTS AND THE ROLE OF CHANCE:** There were 104 healthy children (52%) born in the IVF-SET group, 83 (43%) the IVF-MNC group and 97 (47%) in the IUI-COH group. The mean costs per couple were € 7187 for IVF-SET, € 8206 for IVF-MNC and € 5070 for IUI-COH. Compared with IUI-COH, the costs for IVF-SET and IVF-MNC were significantly higher (mean differences € 2117; 95% CI: € 1544-€ 2657 and € 3136, 95% CI: € 2519-€ 3754, respectively). The ICER for IVF-SET compared with IUI-COH was € 43 375 for the birth of an additional healthy child. In the comparison of IVF-MNC to IUI-COH, the latter was the dominant strategy, i.e. more effective at lower costs.

**LIMITATIONS, REASONS FOR CAUTION:** We only report on direct health care costs. The present analysis is limited to 12 months.

**WIDER IMPLICATIONS OF THE FINDINGS:** Since we found no evidence in support of offering IVF as a first-line strategy in couples with unexplained and mild subfertility, IUI-COH should remain the treatment of first choice.

**STUDY FUNDING/COMPETING INTERESTS:** The study was supported by a grant from ZonMw, the Netherlands Organization for Health Research and Development, (120620027) and a grant from Zorgverzekeraars Nederland, the Netherlands' association of health care insurers (09-003).

**TRIAL REGISTRATION NUMBER:** Current Controlled Trials ISRCTN52843371; Nederlands Trial Register NTR939. © The Author 2015. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology. All rights reserved. For Permissions, please email: journals.permissions@oup.com.

**KEYWORDS:** cost-effectiveness; in vitro fertilization; intrauterine insemination; modified natural cycle; single embryo transfer

PMID: 26269539

**Prevention of multiple pregnancies in couples with unexplained or mild male subfertility: randomised controlled trial of in vitro fertilisation with single embryo transfer or in vitro fertilisation in modified natural cycle compared with intrauterine insemination with controlled ovarian hyperstimulation.**

Bensdorp AJ1, Tjon-Kon-Fat RI1, Bossuyt PM2, Koks CA3, Oosterhuis GJ4, Hoek A5, Hompes PG6, Broekmans FJ7, Verhoeve HR8, de Bruin JP9, van Golde R10, Repping S1, Cohlen BJ11, **Lambers MD12**, van Bommel PF13, Slappendel E14, Perquin D15, Smeenk JM16, Pelinck MJ17, Gianotten J18, Hoozemans DA19, Maas JW3, Eijkemans MJ20, van der Veen F1, Mol BW21, van Wely M22.

BMJ. 2015 Jan 9;350:g7771. doi: 10.1136/bmj.g7771.

**OBJECTIVES:** To compare the effectiveness of in vitro fertilisation with single embryo transfer or in vitro fertilisation in a modified natural cycle with that of intrauterine insemination with controlled ovarian hyperstimulation in terms of a healthy child.

**DESIGN:** Multicentre, open label, three arm, parallel group, randomised controlled non-inferiority trial.

SETTING: 17 centres in the Netherlands.

PARTICIPANTS: Couples seeking fertility treatment after at least 12 months of unprotected intercourse, with the female partner aged between 18 and 38 years, an unfavourable prognosis for natural conception, and a diagnosis of unexplained or mild male subfertility.

INTERVENTIONS: Three cycles of in vitro fertilisation with single embryo transfer (plus subsequent cryocycles), six cycles of in vitro fertilisation in a modified natural cycle, or six cycles of intrauterine insemination with ovarian hyperstimulation within 12 months after randomisation.

MAIN OUTCOME MEASURES: The primary outcome was birth of a healthy child resulting from a singleton pregnancy conceived within 12 months after randomisation. Secondary outcomes were live birth, clinical pregnancy, ongoing pregnancy, multiple pregnancy, time to pregnancy, complications of pregnancy, and neonatal morbidity and mortality RESULTS: 602 couples were randomly assigned between January 2009 and February 2012; 201 were allocated to in vitro fertilisation with single embryo transfer, 194 to in vitro fertilisation in a modified natural cycle, and 207 to intrauterine insemination with controlled ovarian hyperstimulation. Birth of a healthy child occurred in 104 (52%) couples in the in vitro fertilisation with single embryo transfer group, 83 (43%) in the in vitro fertilisation in a modified natural cycle group, and 97 (47%) in the intrauterine insemination with controlled ovarian hyperstimulation group. This corresponds to a risk, relative to intrauterine insemination with ovarian hyperstimulation, of 1.10 (95% confidence interval 0.91 to 1.34) for in vitro fertilisation with single embryo transfer and 0.91 (0.73 to 1.14) for in vitro fertilisation in a modified natural cycle. These 95% confidence intervals do not extend below the predefined threshold of 0.69 for inferiority. Multiple pregnancy rates per ongoing pregnancy were 6% (7/121) after in vitro fertilisation with single embryo transfer, 5% (5/102) after in vitro fertilisation in a modified natural cycle, and 7% (8/119) after intrauterine insemination with ovarian hyperstimulation (one sided  $P=0.52$  for in vitro fertilisation with single embryo transfer compared with intrauterine insemination with ovarian hyperstimulation; one sided  $P=0.33$  for in vitro fertilisation in a modified natural cycle compared with intrauterine insemination with controlled ovarian hyperstimulation). CONCLUSIONS: In vitro fertilisation with single embryo transfer and in vitro fertilisation in a modified natural cycle were non-inferior to intrauterine insemination with controlled ovarian hyperstimulation in terms of the birth of a healthy child and showed comparable, low multiple pregnancy rates. Trial registration Current Controlled Trials ISRCTN52843371; Netherlands Trial Register NTR939.

PMID: 25576320

### Results of sling surgery in a non-selected population.

Hogewoning CR1, Oostrom AJ2, **Hogewoning CJ3**, Pelger RC2, Bekker MD2, Putter H4, Elzevier HW2.

Int J Gynaecol Obstet. 2016 Jan;132(1):46-9. doi: 10.1016/j.ijgo.2015.06.053. Epub 2015 Oct 9.

OBJECTIVE: To evaluate sling surgery in terms of effectiveness and quality of life, and describe the effects of confounding variables on outcomes.

METHODS: A retrospective cohort study using multiple validated questionnaires was conducted in a specialized pelvic floor center in the Netherlands. Women were enrolled after undergoing sling surgery between January 1, 2010, and January 31, 2012. In addition to the preoperative questionnaire, participants completed a questionnaire a minimum of 6 weeks after surgery to assess outcomes.

RESULTS: Of 255 eligible participants, 228 (89.4%) returned the postoperative questionnaire

after a mean follow-up of 14.9 months (range 2-32). At the time of follow-up, 158 (69.3%) patients considered themselves cured, and an improvement was observed in 155 (68.9%) patients; 70 (31.1%) patients rated their postoperative situation as little improved, unchanged, or deteriorated. Compared with patients who had no history of previous related surgery, patients with prior sling surgery benefited significantly less from surgery, whereas those with concomitant vaginal surgery showed similar scores in all outcome parameters. A high body mass index was found to have a negative effect on the results of surgery.

**CONCLUSION:** midurethral sling surgery is both efficient and effective in curing stress urinary incontinence. However, patient characteristics and confounding variables can influence the outcome of surgery and should therefore always be discussed with the patient.

**KEYWORDS:** Midurethral sling; Pelvic organ prolapse surgery; Quality of life; Stress-urinary incontinence; Surgery

*PMID: 26482591*

# Interne Geneeskunde

## Angiogenesis- and Hypoxia-Associated Proteins as Early Indicators of the Outcome in Patients with Metastatic Breast Cancer Given First-Line Bevacizumab-Based Therapy.

Lam SW1, Nota NM1, Jager A2, Bos MM3, **van den Bosch J4**, van der Velden AM5, Portielje JE6, Honkoop AH7, van Tinteren H8, Boven E9; Members of the ATX trial team. Clin Cancer Res. 2016 Jan 28. [Epub ahead of print]

**PURPOSE:** We examined whether pretreatment levels of angiogenesis- or hypoxia-related proteins and their changes after one cycle of first-line bevacizumab-based therapy were associated with response, PFS, or OS in patients with metastatic breast cancer.

**EXPERIMENTAL DESIGN:** We included 181 patients enrolled in the phase II ATX trial evaluating first-line paclitaxel and bevacizumab without or with capecitabine (NTR1348). Plasma samples were analyzed for VEGF-A, soluble VEGFR2 (sVEGFR2), angiopoietin 2 (ANG2), soluble TIE2 (sTIE2), IL6, IL8, and carbonic anhydrase 9 (CA9). Baseline serum CA15-3 was documented. HR was adjusted for confounding factors. Where appropriate, an optimal cut-off value defining a high and a low group was determined with Martingale residuals.

**RESULTS:** At baseline, multiple proteins were significantly associated with PFS (ANG2, IL6, IL8, CA9, CA15-3) and OS (ANG2, sTIE2, IL6, IL8, CA9, CA15-3). After one cycle, VEGF-A, ANG2, sTIE2, and IL8 significantly decreased, while sVEGFR2 and CA9 significantly increased. The relative change in sVEGFR2 ( $P = 0.01$ ) and IL8 ( $P = 0.001$ ) was associated with response. Defining optimal cut-off, patients with a high CA9 rise ( $>2.9\%$ ) had better PFS (HR 0.45) and OS (HR 0.54) than those with low/no rise. **CONCLUSIONS:** Multiple angiogenesis- or hypoxia-related proteins were prognostic for PFS and OS. Molecular agents targeting these proteins might be beneficial in patients with high levels. Changes in IL8 or sVEGFR2 levels at second cycle appear predictive for response. Changes in CA9 levels during bevacizumab-based therapy for prediction of PFS and OS merit further study. Clin Cancer Res; 1-10. ©2015 AACR. ©2015 American Association for Cancer Research.

PMID: 26823602

## CD4-Positive T Cells and M2 Macrophages Dominate the Peritoneal Infiltrate of Patients with Encapsulating Peritoneal Sclerosis.

Habib SM1, Abrahams AC2, **Korte MR3**, Zietse R1, de Vogel LL4, Boer WH2, Dendooven A5, Clahsen-van Groningen MC4, Betjes MG1. PLoS One. 2015 Apr 24;10(4):e0120174. doi: 10.1371/journal.pone.0120174. eCollection 2015.

**BACKGROUND:** Encapsulating peritoneal sclerosis (EPS) is a severe complication of peritoneal dialysis (PD). Previously, it has been shown that infiltrating CD4-positive T cells and M2 macrophages are associated with several fibrotic conditions. Therefore, the characteristics of the peritoneal cell infiltrate in EPS may be of interest to understand EPS pathogenesis. In this study, we aim to elucidate the composition of the peritoneal cell infiltrate in EPS patients and relate the findings to clinical outcome.

**STUDY DESIGN, SETTING, AND PARTICIPANTS:** We studied peritoneal membrane biopsies of 23 EPS patients and compared them to biopsies of 15 PD patients without EPS. The cellular infiltrate was characterized by immunohistochemistry to detect T cells (CD3-positive), CD4-positive (CD4+) and CD8-positive T cell subsets, B cells (CD20-positive), granulocytes (CD15-positive), macrophages (CD68-positive), M1 (CD80-positive), and M2 (CD163-positive) macrophages. Tissues were analysed using digital image analysis. Kaplan-Meier survival analysis was performed to investigate the survival in the different staining groups. **RESULTS:** The cellular infiltrate in EPS biopsies was dominated by mononuclear cells. For both CD3 and CD68, the median percentage of area stained was higher in biopsies of EPS as opposed to non-EPS patients ( $p < 0.001$ ). EPS biopsies showed a higher percentage of area stained for CD4 (1.29% (0.61-3.20)) compared to CD8 (0.71% (0.46-1.01),  $p = 0.04$ ), while in the non-EPS group these cells were almost equally represented (respectively 0.28% (0.05-0.83) versus 0.22% (0.17-0.43),  $p = 0.97$ ). The percentage of area stained for both CD80 and CD163 was higher in EPS than in non-EPS biopsies ( $p < 0.001$ ), with CD163+ cells being the most abundant phenotype. Virtually no CD20-positive and CD15-positive cells were present in biopsies of a subgroup of EPS patients. No relation was found between the composition of the mononuclear cell infiltrate and clinical outcome.

**CONCLUSIONS:** A characteristic mononuclear cell infiltrate consisting of CD4+ and CD163+ cells dominates the peritoneum of EPS patients. These findings suggest a role for both CD4+ T cells and M2 macrophages in the pathogenesis of EPS.

PMID: 25910222

### Early home-based group education to support informed decision-making among patients with end-stage renal disease: a multi-centre randomized controlled trial.

Massey EK1, **Gregoor PJ2**, Nette RW3, van den Dorpel MA4, van Kooij A4, Zietse R1, Zuidema WC1, Timman R5, Busschbach JJ5, Weimar W1.

Nephrol Dial Transplant. 2015 Aug 31. pii: gfv322. [Epub ahead of print]

**BACKGROUND:** The aim was to test the effectiveness of early home-based group education on knowledge and communication about renal replacement therapy (RRT).

**METHODS:** We conducted a randomized controlled trial using a cross-over design among 80 end-stage renal disease (ESRD) patients. Between T0 and T1 (weeks 1-4) Group 1 received the intervention and Group 2 received standard care. Between T1 and T2 (weeks 5-8) Group 1 received standard care and Group 2 received the intervention. The intervention was a group education session on RRT options held in the patient's home given by social workers. Patients invited members from their social network to attend. Self-report questionnaires were used at T0, T1 and T2 to measure patients' knowledge and communication, and concepts from the Theory of Planned Behaviour such as attitude. Comparable questionnaires were completed pre-post intervention by 229 attendees. Primary RRT was registered up to 2 years post-intervention. Multilevel linear modelling was used to analyse patient data and paired t-tests for attendee data.

**RESULTS:** Statistically significant increases in the primary targets knowledge and communication were found among patients and attendees after receiving the intervention. The intervention also had a significant effect in increasing positive attitude toward living donation and haemodialysis. Of the 80 participants, 49 underwent RRT during follow-up. Of these, 34 underwent a living donor kidney transplant, of which 22 were pre-emptive.

CONCLUSIONS: Early home-based group education supports informed decision-making regarding primary RRT for ESRD patients and their social networks and may remove barriers to pre-emptive transplantation. © The Author 2015. Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved.

KEYWORDS: kidney transplantation; living donors; patient education; renal dialysis; renal replacement therapy

PMID: 26330561

### **Encapsulating peritoneal sclerosis is associated with T-cell activation.**

Betjes MG1, Habib MS1, Struijk DG2, Lopes Barreto D2, **Korte MR3**, Abrahams AC4, Nagtzaam NM5, Clahsen-van Groningen MC6, Dik WA5, Litjens NH1.

Nephrol Dial Transplant. 2015 Sep;30(9):1568-76. doi: 10.1093/ndt/gfv092. Epub 2015 May 1.

BACKGROUND: Encapsulating peritoneal sclerosis (EPS) is an excessive fibrotic response of the peritoneum that may occur after long-term peritoneal dialysis (PD). The underlying pathophysiology is poorly understood, but involvement of peritoneal inflammatory T helper 1 cells may be pivotal.

METHODS: Soluble interleukin-2 receptor alpha (sCD25) concentration was measured as a marker for T-cell activation in serum and ascites from EPS patients and various control patient groups. Peritoneal biopsies were stained for the presence of T cells, and T cells isolated from ascites of EPS patients were characterized in detail for differentiation status and cytokine expression.

RESULTS: Serum sCD25 concentrations are significantly and specifically increased in EPS patients compared with haemodialysis, PD and predialysis patients. Peritoneal effluent of stable PD patients contains very low levels of sCD25, while sCD25 levels in ascites of EPS patients are high and indicative of local production. In the years preceding the diagnosis of EPS, the serum sCD25 concentrations increased while remaining at stable levels in control PD patients. The peritoneum and ascites of EPS patients showed a significant influx of T cells with relatively increased numbers of CD4+ T cells. These T cells were fully differentiated and displayed a T helper 1 cell type with a pro-inflammatory cytokine profile.

CONCLUSIONS: Increased serum sCD25 concentrations and peritoneal lymphocytosis in EPS patients indicate the involvement of activated T cells in the pathophysiology of excessive fibrosis.

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KEYWORDS: T cells; biomarker; encapsulating peritoneal sclerosis; peritoneal dialysis; sCD25

PMID: 25934991

### **Examination of peripheral blood smears: performance evaluation of a digital microscope system using a large-scale leukocyte database.**

**Stouten K1,2, Riedl JA3, Levin MD2, van Gelder W1**

Int J Lab Hematol. 2015 Oct;37(5):e137-40. doi: 10.1111/ijlh.12391. Epub 2015 Jun 8.

PMID: 26059017

### **Interlaboratory Reproducibility of Blood Morphology Using the Digital Microscope.**

**Riedl JA1, Stouten K2,** Ceelie H3, Boonstra J4, **Levin MD5,** van Gelder W6.

J Lab Autom. 2015 Dec;20(6):670-5. doi: 10.1177/2211068215584278. Epub 2015 Apr 29.

Differential counting of peripheral blood cells is an important diagnostic tool. However, manual morphological analysis using the microscope is time-consuming and requires highly trained personnel. The digital microscope is capable of performing an automated peripheral blood cell differential, which is as reliable as manual classification by experienced laboratory technicians. To date, information concerning the interlaboratory variation and quality of cell classification by independently operated digital microscopy systems is limited. We compared four independently operated digital microscope systems for their ability in classifying the five main peripheral blood cell classes and detection of blast cells in 200 randomly selected samples. Set against the averaged results, the R2 values for neutrophils ranged between 0.90 and 0.96, for lymphocytes between 0.83 and 0.94, for monocytes between 0.77 and 0.82, for eosinophils between 0.70 and 0.78, and for blast cells between 0.94 and 0.99. The R2 values for the basophils were between 0.28 and 0.34. This study shows that independently operated digital microscopy systems yield reproducible preclassification results when determining the percentages of neutrophils, eosinophils, lymphocytes, monocytes, and blast cells in a peripheral blood smear. Detection of basophils was hampered by the low incidence of this cell class in the samples.

© 2015 Society for Laboratory Automation and Screening.

KEYWORDS: blood differential; digital microscopy; hematology; preclassification

PMID: 25925737

### **Multi-center randomized open label phase II trial on three rituximab dosing schemes in immune thrombocytopenia patients.**

Zwaginga JJ1, van der Holt B2, Te Boekhorst PA3, Biemond BJ4, **Levin MD5,** van der Griend R6, Brand A7, Zweegman S8, Pruijt HF9, Novotny VM10, Vreugdenhil A11, de Groot MR12, de Weerd O13, van Pampus EC14, van Maanen-Lamme TM15, Wittebol S16, Schipperus MR17, Silbermann MH18, Huijgens PC8, Luten M2, Hollestein R2, Brakenhoff JA19, Schrama JG20, Valster FA21, Velders GA22, Koene HR13; Dutch HOVON 64 study group.

Haematologica. 2015 Mar;100(3):e90-2. doi: 10.3324/haematol.2014.110213.

Epub 2014 Nov 25.

KEYWORDS: early response; immune thrombocytopenia; open label phase II; rituximab; splenectomy delaying

PMID: 25425692

### **[Nephrotic syndrome in Crohn's disease].**

**Boiten HJ1, Honkoop P, Smak Gregoor PJ.**

Ned Tijdschr Geneeskd. 2015;159(0):A9264.

BACKGROUND: The differential diagnosis of nephrotic syndrome is diverse. Systemic conditions and medication such as NSAIDs can cause this syndrome.

CASE DESCRIPTION: A 33-year-old male with Crohn's disease for which he was receiving adalimumab noticed he was gaining weight and had swollen ankles. Examination revealed nephrotic syndrome without renal insufficiency. Renal biopsy showed a membranous glomerulonephritis.

ropathy. We excluded secondary causes of membranous glomerulopathy such as diabetes mellitus, systemic lupus erythematosus, viral infection or malignancy. We treated the patient with high-dose glucocorticoids on a weaning schedule and adalimumab was discontinued.

This regimen resulted in complete remission. It is likely that the nephrotic syndrome with membranous glomerulopathy was associated with adalimumab.

**CONCLUSION:** In patients with nephrotic syndrome based on membranous glomerulopathy both primary and secondary causes, such as use of medication, need to be excluded.

PMID: 26306485

### **Ofatumumab maintenance versus observation in relapsed chronic lymphocytic leukaemia (PROLONG): an open-label, multicentre, randomised phase 3 study.**

van Oers MH1, Kuliczkowski K2, Smolej L3, Petrini M4, Offner F5, Grosicki S6, **Levin MD7**, Gupta I8, Phillips J8, Williams V9, Manson S10, Lisby S11, Geisler C12; PROLONG study investigators.

Lancet Oncol. 2015 Oct;16(13):1370-9. doi: 10.1016/S1470-2045(15)00143-6.

Epub 2015 Sep 13.

**BACKGROUND:** Ofatumumab is a human anti-CD20 monoclonal antibody that has proven efficacy as monotherapy in refractory chronic lymphocytic leukaemia. We assessed the efficacy and safety of ofatumumab maintenance treatment versus observation for patients in remission after re-induction treatment for relapsed chronic lymphocytic leukaemia.

**METHODS:** This open-label, multicentre, randomised phase 3 study enrolled patients aged 18 years or older from 130 centres in 24 countries who had chronic lymphocytic leukaemia in complete or partial remission after second-line or third-line treatment. Eligible patients had a WHO performance status of 0-2, had a response assessment within the previous 3 months, did not have refractory disease, autoimmune haemolytic anaemia requiring treatment, chronic or active infection requiring treatment, and had not previously received maintenance treatment or autologous or allogeneic stem-cell transplant. Using a randomisation list generated by a central computerised system and an interactive voice recognition system, we randomly assigned (1:1) patients to receive ofatumumab (300 mg followed by 1000 mg 1 week later and every 8 weeks for up to 2 years) or undergo observation. Randomisation was stratified by number and type of previous treatment and remission status after induction treatment (block size of four). Treatment assignment was open label. The primary endpoint was investigator-assessed progression-free survival in the intention-to-treat population. We report the results of a prespecified interim analysis after two-thirds of the planned study events (disease progression or death) had happened. This trial is closed to accrual but follow-up is ongoing. This trial is registered with ClinicalTrials.gov, number NCT00802737.

**FINDINGS:** Between May 6, 2010, and June 19, 2014, we enrolled 474 patients: 238 patients were randomly assigned to receive ofatumumab maintenance treatment and 236 to undergo observation. One (<1%) patient in the ofatumumab group did not receive the allocated intervention (withdrawal of consent). The median follow-up was 19.1 months (IQR 10.3-28.8). Progression-free survival was improved in patients assigned to the ofatumumab group (29.4 months, 95% CI 26.2-34.2) compared with those assigned to observation (15.2 months, 11.8-18.8; hazard ratio 0.50, 95% CI 0.38-0.66;  $p < 0.0001$ ). The most common grade 3 or higher adverse events up to 60 days after last treatment were neutropenia (56 [24%] of 237 patients in the ofatumumab group vs 23 [10%] of 237 in the observation group) and infections (31 [13%] vs 20 [8%]). 20 (8%) of 237 patients in the ofatumumab group and three (1%) of 237 patients in the observation group had adverse events that led to permanent discontinuation

of treatment. Up to 60 days after last treatment, two deaths related to adverse events occurred in the ofatumumab treatment group and five deaths related to adverse events occurred in the observation group; no deaths were attributed to the study drug.

INTERPRETATION: These data are important for the development of optimum maintenance strategies in patients with relapsed chronic lymphocytic leukaemia, notably in the present era of targeted drugs, many of which are to be used until progression.

FUNDING: GlaxoSmithKline and Genmab.

PMID: 26377300

### **Spontaneous sternal fracture due to multiple myeloma requiring extensive surgical repair.**

**Reuling EM1, Jakma TS1, Schnater JM1, Westerweel PE2.**

BMJ Case Rep. 2015 Nov 30;2015. pii: bcr2015211498. doi: 10.1136/bcr-2015-211498.

Spontaneous sternal fracture is a well-known complication of multiple myeloma due to osteolytic bone lesions. The possibility of a multiple myeloma should be thoroughly investigated in patients presenting with a spontaneous sternal fracture. This work up should go beyond protein electrophoresis alone as a monoclonal paraprotein is not always present. In some cases, the myeloma plasma cell clone produces only the free light chain ( $\kappa$  or  $\lambda$ ) or may even be non-secretory. The underlying plasma cell dyscrasia is treated with chemotherapy and, if needed, local radiotherapy. However, for patients with a fracture causing persistent pain and physical discomfort, internal fixation may be additionally required. We present a case of a patient who presented with a displaced pathological sternal fracture. She was treated with chemotherapy, radiotherapy and an open reduction and internal fixation with a Locking Compression Plate (LCP). This technique offers a feasible option for rigid fixation of pathological fractures.

PMID: 26621901

# Keel-, Neus- en Oorheelkunde

## Biofilm formation on the Provox ActiValve: Composition and ingrowth analyzed by Illumina paired-end RNA sequencing, fluorescence in situ hybridization and confocal laser scanning microscopy.

Timmermans AJ1, Harmsen HJ2, Bus-Spoor C2, **Buijssen KJ3**, van As-Brooks C1,4, de Goffau MC2, Tonk RH2, van den Brekel MW1,5,6, Hilgers FJ1,5,6, van der Laan BF7. Head Neck. 2015 Jan 12. doi: 10.1002/hed.24014. [Epub ahead of print]

**BACKGROUND:** The most frequent cause of voice prosthesis failure is microbial biofilm formation on the silicone valve, leading to destruction of the material and transprosthetic leakage. The Provox ActiValve valve is made of fluoroplastic, which should be unsusceptible to destruction. The purpose of this study was to determine if fluoroplastic is unsusceptible to destruction by *Candida* species.

**METHODS:** Thirty-three dysfunctional Provox ActiValves (collected 2011-2013). Biofilm analysis was performed with Illumina paired-end sequencing (IPES), assessment of biofilm-material interaction with fluorescence in situ hybridization (FISH), and confocal laser scanning microscopy (CLSM).

**RESULTS:** IPES (n = 10) showed that *Candida albicans* and *Candida tropicalis* are dominant populations on fluoroplastic and silicone. Microbial diversity is significantly lower on fluoroplastic. *Lactobacillus gasseri* is the prevalent bacterial strain on most voice prostheses. FISH and CLSM (n = 23): in none of the cases was ingrowth of *Candida* species present in the fluoroplastic.

**CONCLUSION:** Fluoroplastic material of Provox ActiValve seems unsusceptible to destruction by *Candida* species, which could help improve durability of voice prostheses. © 2015 Wiley Periodicals, Inc. Head Neck, 2015.

**KEYWORDS:** *Candida*; biofilm; total laryngectomy; voice prosthesis; voice rehabilitation

PMID: 25641597

# Kindergeneeskunde

## **A 7-year-old boy with fever, rash and coughing. Erythema multiforme (EM) major.**

**van der Bent SA1, van Ham-Borawitz VE, de Kleijn ED, Reeder SW, Laeijendecker R.**  
Neth J Med. 2015 Jul;73(6):302-3.

PMID: 26228199

## **Components of the metabolic syndrome in early childhood in very-low-birth-weight infants and term small and appropriate for gestational age infants.**

**de Jong M1, Cranendonk A2, van Weissenbruch MM2.**

Pediatr Res. 2015 Oct;78(4):457-61. doi: 10.1038/pr.2015.118. Epub 2015 Jun 18.

**BACKGROUND:** Term small-for-gestational-age (SGA) and preterm born infants have an increased prevalence of metabolic syndrome components already in childhood. Our recent study in 2-year-old very-low-birth-weight (VLBW) infants was limited by the absence of a control group of term born children. We compared the metabolic syndrome components in early childhood in VLBW and term SGA infants to term appropriate for gestational age (AGA) infants. **METHODS:** We included 38 VLBW children and 82 term born children (64 AGA/18 SGA). HDL cholesterol, triglycerides, glucose and insulin were measured in blood samples taken at 1 year (term children) and 2 years (all children) of (corrected) age. **RESULTS:** At 2 years corrected age VLBW children have lower BMI and higher glucose level compared to AGA children. SGA children have lower BMI at 1 and 2 years of age and a high prevalence of high triglyceride levels at 1 year of age compared to AGA children. Total body fat is a significant determinant of HDL cholesterol and triglycerides and birth weight is a significant determinant of glucose at 2 years corrected age. **CONCLUSION:** In early childhood VLBW and term SGA children already have a high prevalence of some metabolic syndrome components compared to term AGA children. *Pediatric Research* (2015); doi:10.1038/pr.2015.118.

PMID: 26086641

## **Long-term effects of oxandrolone treatment in childhood on neurocognition, quality of life and social-emotional functioning in young adults with Turner syndrome.**

**Freriks K1, Verhaak CM2, Sas TC3, Menke LA4, Wit JM4, Otten BJ5, de Muinck Keizer-Schrama SM6, Smeets DF7, Netea-Maier RT8, Hermus AR8, Kessels RP9, Timmers HJ8.**  
Horm Behav. 2015 Mar;69:59-67. doi: 10.1016/j.yhbeh.2014.12.008. Epub 2015 Jan 3.

Turner syndrome (TS) is the result of (partial) absence of one X-chromosome. Besides short stature, gonadal dysgenesis and other physical aspects, TS women have typical psychological features. Since psychological effects of androgen exposure in childhood probably are long-lasting, we explored long-term psychological functioning after oxandrolone (Ox) therapy during childhood in adults with TS in terms of neurocognition, quality of life and social-emotional

functioning. During the initial study, girls were treated with growth hormone (GH) combined with placebo (Pl), Ox 0.03mg/kg/day, or Ox 0.06mg/kg/day from the age of eight, and estrogen from the age of twelve. Sixty-eight women participated in the current double-blinded follow-up study (mean age 24.0y, mean time since stopping GH/Ox 8.7y). We found no effects on neurocognition. Concerning quality of life women treated with Ox had higher anxiety levels (STAI 37.4±8.4 vs 31.8±5.0, p0.002) and higher scores on the depression subscale of the SCL-90-R (25.7±10.7 vs 20.5±4.7, p0.01). Regarding social-emotional functioning, emotion perception for fearful faces was lower in the Ox-treated patients, without effect on interpersonal behavior. Our exploratory study is the first to suggest that androgen treatment in adolescence possibly has long-term effects on adult quality of life and social-emotional functioning. However, differences are small and clinical implications of our results seem limited. Therefore we would not recommend against the use of Ox in light of psychological consequences.

PMID: 25562712

### Reference intervals for renal injury biomarkers neutrophil gelatinase-associated lipocalin and kidney injury molecule-1 in young infants.

Zwiers AJ, de Wildt SN, de Rijke YB, Willemsen SP, **Abdullahi NS**, Tibboel D, Cransberg K. Clinical Chemistry and Laboratory Medicine (CCLM). DOI: 10.1515/cclm-2014-1020, February 2015

Background: Reliable reference intervals for two novel urinary biomarkers of renal injury, neutrophil gelatinase-associated lipocalin (uNGAL) and kidney injury molecule-1 (uKIM-1) are lacking for infants. Therefore, the aim of our study was to establish reference intervals for urinary NGAL and KIM-1 absolute concentrations as well as normalized to urinary creatinine in young infants categorized in small age intervals.

Methods: From June 2010 to March 2014, serum and urine samples of 106 basically healthy infants (born between 37 and 42 weeks of gestation) aged 1 day to 1 year were collected. Blood samples were assayed for serum creatinine levels to confirm a healthy renal status. Urine samples were assayed for creatinine, uNGAL (ng/mL) and uKIM-1 (ng/mL).

Results: Two thirds of the study cohort were boys. uNGAL concentrations declined with increasing age (likelihood ratio test, p=0.001). Also, uNGAL concentrations were higher in girls (50th centile uNGAL was 27.1 ng/mL) than boys (50th centile uNGAL was 14.3 ng/mL) (two tailed Wald test, p<0.001) NGAL concentrations were not related to ethnicity. uKIM-1 concentrations were extremely low in almost all 106 subjects [median uKIM-1 was 0.08 (IQR 0.08–0.08) ng/mL] and not related with age, gender or ethnicity (all p>0.05).

Conclusions: Our data uniquely provide uNGAL and uKIM-1 reference intervals for the first year of life. Notably, only uNGAL levels decreased with increasing age and were higher in girls. These reference intervals enable future studies to evaluate the performance of both biomarkers in detecting early kidney tubular injury, particularly in the setting of critical care.

Keywords: kidney injury molecule-1 (KIM-1); neutrophil gelatinase-associated lipocalin (NGAL); pediatrics; reference intervals; serum creatinine; urinary biomarkers

PMID: 25720126

### Salivary and serum cortisol and relation to blood pressure in infancy and early childhood in very-low-birth-weight infants.

**de Jong M1**, Cranendonk A2, van Weissenbruch MM2.

Pediatr Res. 2015 Oct;78(4):476-9. doi: 10.1038/pr.2015.128. Epub 2015 Jul 7.

**BACKGROUND:** Programming of the hypothalamic-pituitary-adrenal (HPA) axis possibly explains the relation between intrauterine growth restriction (IUGR) and/or preterm birth and elevated blood pressure in later life. Very-low-birth-weight infants (birth weight <1,500 g) have high prevalence of raised blood pressure, already in early childhood. We investigated cortisol levels, relation to blood pressure and reliability of salivary cortisol in infancy and early childhood in very-low-birth-weight infants.

**METHODS:** We included 41 children, participating in the randomized controlled Neonatal Insulin Replacement Therapy in Europe (NIRTURE) trial. Serum and salivary samples for cortisol measurement (immunoassay) were taken simultaneously at 6 mo and separately at 2 y corrected age. Blood pressure was measured at 2 y corrected age.

**RESULTS:** Serum cortisol was significantly correlated to systolic and diastolic blood pressure in boys and in the early-insulin treated group. At 2 y corrected age serum cortisol was significantly higher in the early-insulin group compared to the standard care group. At 6 mo corrected age salivary cortisol was significantly correlated to serum cortisol.

**CONCLUSION:** In very-low-birth-weight boys, the positive correlation between cortisol and blood pressure is present at 2 y corrected age. Early insulin therapy could affect programming of the HPA axis. Salivary cortisol mirrors serum levels at 6 mo corrected age. *Pediatric Research* (2015); doi:10.1038/pr.2015.128.

*PMID: 26151494*

## **Automated detection and classification of teardrop cells by a novel RBC module using digital imaging/microscopy.**

**Egelé A1, van Gelder W2, Riedl J2.**

Int J Lab Hematol. 2015 Jun 29. doi: 10.1111/ijlh.12399. [Epub ahead of print]

PMID: 26118701

## **Examination of peripheral blood smears: performance evaluation of a digital microscope system using a large-scale leukocyte database.**

**Stouten K1,2, Riedl JA3, Levin MD2, van Gelder W1**

Int J Lab Hematol. 2015 Oct;37(5):e137-40. doi: 10.1111/ijlh.12391. Epub 2015 Jun 8.

PMID: 26059017

## **Interlaboratory Reproducibility of Blood Morphology Using the Digital Microscope.**

**Riedl JA1, Stouten K2, Ceelie H3, Boonstra J4, Levin MD5, van Gelder W6.**

J Lab Autom. 2015 Dec;20(6):670-5. doi: 10.1177/2211068215584278. Epub 2015 Apr 29.

Differential counting of peripheral blood cells is an important diagnostic tool. However, manual morphological analysis using the microscope is time-consuming and requires highly trained personnel. The digital microscope is capable of performing an automated peripheral blood cell differential, which is as reliable as manual classification by experienced laboratory technicians. To date, information concerning the interlaboratory variation and quality of cell classification by independently operated digital microscopy systems is limited. We compared four independently operated digital microscope systems for their ability in classifying the five main peripheral blood cell classes and detection of blast cells in 200 randomly selected samples. Set against the averaged results, the R2 values for neutrophils ranged between 0.90 and 0.96, for lymphocytes between 0.83 and 0.94, for monocytes between 0.77 and 0.82, for eosinophils between 0.70 and 0.78, and for blast cells between 0.94 and 0.99. The R2 values for the basophils were between 0.28 and 0.34. This study shows that independently operated digital microscopy systems yield reproducible preclassification results when determining the percentages of neutrophils, eosinophils, lymphocytes, monocytes, and blast cells in a peripheral blood smear. Detection of basophils was hampered by the low incidence of this cell class in the samples.

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KEYWORDS: blood differential; digital microscopy; hematology; preclassification

PMID: 25925737

# Klinische Fysica

## **Coaching Reduced the Radiation Dose of Pain Physicians by Half during Interventional Procedures.**

**Slegers AS<sup>1</sup>, Gültuna I, Aukes JA, van Gorp EJ, Blommers FM, Niehof SP, Bosman J.**

Pain Pract. 2015 Jun;15(5):400-6. doi: 10.1111/papr.12251. Epub 2014 Oct 29.

The increased use of C-arm fluoroscopy in interventional pain management has led to higher radiation exposure for pain physicians. This study investigated whether or not real-time radiation dose feedback with coaching can reduce the scatter dose received by pain physicians. Firstly, phantom measurements were made to create a scatter dose profile, which visualizes the average scatter radiation for different C-arm positions at 3 levels of height. Secondly, in the clinical part, the radiation dose received by pain physicians during pain treatment procedures was measured real-time to evaluate (1) the effect of real-time dose feedback on the received scatter dose, and (2) the effect of knowledge of the scatter dose profile and active coaching, on the scatter dose received by the pain physician. The clinical study included 330 interventional pain procedures. The results showed that real-time feedback of the received dose did not lead to a reduction in scatter radiation. However, visualization of the scatter dose in a scatter dose profile and active coaching on optimal positions did reduce the scatter radiation received by pain physicians during interventional pain procedures by 46.4% ( $P = 0.05$ ). Knowledge of and real-time coaching with the scatter dose profile reduced the dose of pain physicians by half, caused by their increased awareness for scatter radiation and their insight into strategic positioning.

PMID: 25354342

## **“Should I prioritize medical problem solving or attentive listening?”: the dilemmas and challenges that medical students experience when learning to conduct consultations.**

Aper L1, Veldhuijzen W2, Dornan T3, **van de Ridder M4**, Koole S5, Derese A5, Reniers J5. Patient Educ Couns. 2015 Jan;98(1):77-84. doi: 10.1016/j.pec.2014.09.016. Epub 2014 Oct 5.

**OBJECTIVE:** Communication skills can be trained alongside clinical reasoning, history taking or clinical examination skills. This is advocated as a solution to the low transfer of communication skills. Still, students have to integrate the knowledge/skills acquired during different curriculum parts in patient consultations at some point. How do medical students experience these integrated consultations within a simulated environment and in real practice when dealing with responsibility?

**METHODS:** Six focus groups were conducted with (pre-)/clerkship students.

**RESULTS:** Students were motivated to practice integrated consultations with simulated patients and felt like ‘real physicians’. However, their focus on medical problem solving drew attention away from improving their communication skills. Responsibility for real patients triggered students’ identity development. This identity formation guided the development of an own consultation style, a process that was hampered by conflicting demands of role models. **CONCLUSION:** Practicing complete consultations results in the dilemma of prioritizing medical problem solving above attention for patient communication. Integrated consultation training advances this dilemma to the pre-clerkship period. During clerkships this dilemma is heightened because real patients trigger empathy and responsibility, which invites students to define their role as doctor.

**PRACTICE IMPLICATIONS:** When training integrated consultations, educators should pay attention to students’ learning priorities and support the development of students’ professional identity.

**KEYWORDS:** Communication skills; Conducting consultations; Identity development; Undergraduate medical students

PMID: 25448312

## **Variables that affect the process and outcome of feedback, relevant for medical training: a meta-review.**

**van de Ridder JM1**, McGaghie WC2, Stokking KM3, Ten Cate OT4. Med Educ. 2015 Jul;49(7):658-73. doi: 10.1111/medu.12744.

**CONTEXT:** Feedback is considered important in medical education. The literature is not clear about the mechanisms that contribute to its effects, which are often small to moderate and at times contradictory. A variety of variables seem to influence the impact of feedback on learning. The aim of this study was to determine which variables influence the process and outcomes of feedback in settings relevant to medical education.

**METHODS:** A myriad of studies on feedback have been conducted. To determine the most researched variables, we limited our review to meta-analyses and literature reviews published

in the period from January 1986 to February 2012. According to our protocol, we first identified features of the feedback process that influence its effects and subsequently variables that influence these features. We used a chronological model of the feedback process to categorise all variables found.

**RESULTS:** A systematic search of ERIC, PsycINFO and MEDLINE yielded 1101 publications, which we reduced to 203, rejecting papers on six exclusion criteria. Of these, 46 met the inclusion criteria. In our four-phase model, we identified 33 variables linked to task performance (e.g. task complexity, task nature) and feedback reception (e.g. self-esteem, goal-setting behaviour) by trainees, and to observation (e.g. focus, intensity) and feedback provision (e.g. form, content) by supervisors that influence the subsequent effects of the feedback process. Variables from all phases influence the feedback process and effects, but variables that influence the quality of the observation and rating of the performance dominate the literature. There is a paucity of studies addressing other, seemingly relevant variables.

**CONCLUSIONS:** The larger picture of variables that influence the process and outcome of feedback, relevant for medical education, shows many open spaces. We suggest that targeted studies be carried out to expand our knowledge of these important aspects of feedback in medical education.

*PMID: 26077214*

# Longgeneeskunde

## Is the current diagnostic algorithm reliable for selecting cases for EGFR- and KRAS-mutation analysis in lung cancer?

Vincenten JP<sup>1</sup>, Smit EF<sup>2</sup>, Grünberg K<sup>3</sup>, Postmus PE<sup>4</sup>, Snijders PJ<sup>3</sup>, Witte BI<sup>5</sup>, Heideman DA<sup>3</sup>, Thunnissen E<sup>3</sup>.

Lung Cancer. 2015 Jul;89(1):19-26. doi: 10.1016/j.lungcan.2015.04.005. Epub 2015 Apr 20.

**OBJECTIVES:** Adenocarcinoma (ADC) of the lung may harbor EGFR- or KRAS-mutations, which are relevant for treatment decisions. There is no consensus on the percentages of EGFR- and KRAS-mutations that are allowed to be missed by a diagnostic algorithm, although a percentage of less than 1% for EGFR-mutations has been suggested. The current guidelines do not advise to perform EGFR-mutation analysis in unequivocal squamous cell carcinoma (SqCC). For KRAS-mutations no threshold for missing cases is suggested yet. To improve segregation between ADC and SqCC in small samples, the classification of lung cancer was updated in 2011, adding immunohistochemistry (IHC) for p63 and TTF-1 to the diagnostic algorithm. In this study we examined how many cases with an EGFR- or KRAS-mutation in our database would have been missed, if the current guideline for selecting cases for mutation analysis would have been applied.

**MATERIALS AND METHODS:** From an institutional lung cancer database of specimens analyzed for EGFR- and KRAS-mutations (n=816), cases harboring a mutation without being treated prior with an EGFR-TKI were selected (n=336). Corresponding original histological diagnoses and IHC for TTF-1, p63 and PAS-D were collected. Cases with SqCC on HE or with an IHC pattern favoring SqCC were reassessed according to the criteria of the 2011-classification.

**RESULTS:** From the 336 cases 70% had a KRAS-mutation and 30% an EGFR-mutation.

The number of cases with SqCC on HE and/or an IHC-profile favoring SqCC was 12. After the reassessment six specimens (1.8%) would not have been tested for EGFR-/KRAS-mutations, if the current diagnostic algorithm had been used: 2.0% of EGFR-mutations and 1.7% KRAS-mutations. All six cases were NSCLC with an IHC-profile favoring SqCC.

**CONCLUSION:** Most NSCLC-cases with EGFR- and KRAS-mutations are selected by the current diagnostic algorithm. As a small but relevant fraction is missed, there is room for improvement.

**KEYWORDS:** Adenocarcinoma; EGFR-mutation; Immunohistochemistry; KRAS-mutation; Lung cancer; Squamous cell carcinoma; p40; p63

PMID: 25982011

## SMAD2 Mutations are Associated With Arterial Aneurysms and Dissections.

Micha D<sup>1</sup>, Guo DC<sup>2</sup>, Hilhorst-Hofstee Y<sup>3</sup>, van Kooten F<sup>4</sup>, Atmaja D<sup>1,5</sup>, Overwater E<sup>1,6</sup>, Cayami FK<sup>1,5</sup>, Regalado ES<sup>2</sup>, van Uffelen R<sup>7</sup>, Venselaar H<sup>8</sup>, Faradz SM<sup>5</sup>, Vriend G<sup>8</sup>, Weiss MM<sup>1</sup>, Siermans EA<sup>1</sup>, Maugeri A<sup>1</sup>, Milewicz DM<sup>2</sup>, Pals G<sup>1</sup>, van Dijk FS<sup>1</sup>.

Hum Mutat. 2015 Aug 6. doi: 10.1002/humu.22854. [Epub ahead of print]

We report three families with arterial aneurysms and dissections in which variants predicted to be pathogenic were identified in SMAD2. Moreover, one variant occurred de novo in a

proband with unaffected parents. SMAD2 is a strong candidate gene for arterial aneurysms and dissections given its role in the TGF- $\beta$  signaling pathway. Furthermore, although SMAD2 and SMAD3 probably have functionally distinct roles in cell signaling, they are structurally very similar. Our findings indicate that SMAD2 mutations are associated with arterial aneurysms and dissections and are in accordance with the observation, that patients with pathogenic variants in genes encoding proteins involved in the TGF- $\beta$  signaling pathway, exhibit arterial aneurysms and dissections as key features This article is protected by copyright. All rights reserved.

KEYWORDS: SMAD2; TGF- $\beta$ ; aneurysm; dissection

PMID: 26247899

# Maag-, Darm- en Levergeneeskunde

## Adherence to surveillance guidelines after removal of colorectal adenomas: a large, community-based study.

van Heijningen EM1, Lansdorp-Vogelaar I1, Steyerberg EW1, Goede SL1, Dekker E2, **Lesterhuis W3**, Ter Borg F4, Vecht J5, Spoelstra P6, Engels L7, Bolwerk CJ8, Timmer R9, Kleibeuker JH10, Koornstra JJ10, de Koning HJ1, Kuipers EJ11, van Ballegooijen M1. Gut. 2015 Oct;64(10):1584-92. doi: 10.1136/gutjnl-2013-306453. Epub 2015 Jan 13.

**OBJECTIVE:** To determine adherence to recommended surveillance intervals in clinical practice. **DESIGN:** 2997 successive patients with a first adenoma diagnosis (57% male, mean age 59 years) from 10 hospitals, who underwent colonoscopy between 1998 and 2002, were identified via Pathologisch Anatomisch Landelijk Geautomatiseerd Archief: Dutch Pathology Registry. Their medical records were reviewed until 1 December 2008. Time to and findings at first surveillance colonoscopy were assessed. A surveillance colonoscopy occurring within  $\pm 3$  months of a 1-year recommended interval and  $\pm 6$  months of a recommended interval of 2 years or longer was considered appropriate. The analysis was stratified by period per change in guideline (before 2002: 2-3 years for patients with 1 adenoma, annually otherwise; in 2002: 6 years for 1-2 adenomas, 3 years otherwise). We also assessed differences in adenoma and colorectal cancer recurrence rates by surveillance timing.

**RESULTS:** Surveillance was inappropriate in 76% and 89% of patients diagnosed before 2002 and in 2002, respectively. Patients eligible under the pre-2002 guideline mainly received surveillance too late or were absent (57% of cases). For patients eligible under the 2002 guideline surveillance occurred mainly too early (48%). The rate of advanced neoplasia at surveillance was higher in patients with delayed surveillance compared with those with too early or appropriate timed surveillance (8% vs 4-5%,  $p < 0.01$ ).

**CONCLUSIONS:** There is much room for improving surveillance practice. Less than 25% of patients with adenoma receive appropriate surveillance. Such practice seriously hampers the effectiveness and efficiency of surveillance, as too early surveillance poses a considerable burden on available resources while delayed surveillance is associated with an increased rate of advanced adenoma and especially colorectal cancer. Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to <http://group.bmj.com/group/rights-licensing/permissions>.

**KEYWORDS:** COLONOSCOPY; COLORECTAL ADENOMAS; ENDOSCOPIC POLYPECTOMY; SURVEILLANCE

PMID: 25586057

## Benefit for earlier anti-TNF treatment on IBD disease complications?

Nuij VJ1, Fuhler GM2, Edel MJ2, Ouwendijk RJ3, Rijk MC4, **Beukers R5**, Quispel R6, van Tilburg AJ7, Tang TJ8, Smalbraak H9, Bruin KF10, Lindenburg F11, Peyrin-Biroulet L12, van der Woude CJ2.

J Crohns Colitis. 2015 Jul 29. pii: jjv130. [Epub ahead of print]

**BACKGROUND:** Anti-Tumor Necrosis Factor (anti-TNF) treatment was demonstrated to have disease modifying abilities in IBD. With this study, we aimed to determine the effect of anti-TNF timing on IBD-disease complications and mucosal healing (MH).

**METHODS:** The following IBD-related complications were tested in relation to timing of anti-TNF therapy start in newly diagnosed IBD patients (n=413): fistula formation, abscess formation, EIM, surgery, referral to academic center and MH.

**RESULTS:** Eighty-five patients (21%) received anti-TNF (66 CD, 16 UC, 3 IBDU) of whom 57% (48 pts) < 16 months after diagnosis. Patients receiving anti-TNF early (<16 months) did not differ from patients receiving anti-TNF late (>16 months) regarding gender, age, smoking status and familial IBD. More importantly, patients receiving anti-TNF early did not suffer less IBD-related complications during follow-up as compared to patients started on anti-TNF late, nor was more MH observed. Similar results were obtained when anti-TNF treated patient were stratified more stringently, i.e. <12 months (40 pts) vs. >24 months (24 pts). Cox-regression analysis showed no beneficial correlations between anti-TNF timing and IBD-related complications. Anti-TNF treated patients achieving MH were 11 times less likely to develop EIMs compared to patients who did not achieved MH while on anti-TNF.

**CONCLUSION:** This study was unable to confirm a benefit for earlier anti-TNF treatment on IBD-disease complications. This could be explained by more aggressive treatment earlier in disease, resulting in fewer IBD complications. However, it seems more likely that inappropriate selection of patients for therapy leads to suboptimal treatment and subsequently outcome.

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**KEYWORDS:** anti-TNF; disease complications; inflammatory bowel disease

PMID: 26223842

### **Cost Efficacy of Metal Stents for Palliation of Extrahepatic Bile Duct Obstruction in a Randomized Controlled Trial.**

Walter D1, van Boeckel PG2, Groenen MJ3, Weusten BL4, Witteman BJ5, Tan G6, Brink MA7, Nicolai J8, Tan AC9, **Alderliesten J10**, Venneman NG11, Laleman W12, Jansen JM13, Bodelier A14, Wolters FL15, van der Waaij LA16, Breumelhof R17, Peters FT18, Scheffer RC19, Leenders M2, Hirdes MM2, Steyerberg EW20, Vleggaar FP2, Siersema PD2. *Gastroenterology*. 2015 Jul;149(1):130-8. doi: 10.1053/j.gastro.2015.03.012. Epub 2015 Mar 17.

**BACKGROUND:** & Aims: Endoscopic stents are placed for palliation of extra-hepatic bile duct obstruction. Although self-expandable metals stents (SEMS) remain patent longer than plastic stents, they are more expensive. We aimed to evaluate which type of stent (plastic, uncovered [uSEMS], or partially covered [pcSEMS]), is most effective and assessed costs.

**METHODS:** We performed a multi-center randomized trial in 219 patients at 18 hospitals in the Netherlands from February 2008 through February 2013. Patients were randomly assigned for placement of a plastic stent (n=73), uSEMS (n=75), or pcSEMS (n=71) during endoscopic retrograde cholangiopancreatography. Patients were followed for up to 1 y. Researchers were not blinded to groups. The main study endpoints included functional stent time and costs.

**RESULTS:** The mean functional stent times were 172 days for plastic stents, 288 days for uSEMS, and 299 days for pcSEMS (P<.005 for uSEMS and pSEMS vs plastic). Initial placement of plastic stents (€1042 or \$1106) cost significantly less than of SEMS (€1973 or \$2094) (P=.001). However, the total cost per patient at the end of the follow-up period did not differ significantly

between plastic stents (€7320 or \$7770) and SEMS (€6932 or \$7356) ( $P=.61$ ). Furthermore, in patients with short survival times ( $\leq 3$  months) or metastatic disease, total cost per patient did not differ between plastic stents and SEMS. No differences in costs were found between pcSEMS and uSEMS.

CONCLUSION: Although placement of SEMS (uncovered or partially covered) for palliation of extra-hepatic bile duct obstruction is initially more expensive than placement of plastic stents, SEMS have longer functional time. Total costs after 1 y do not differ significantly with stent type. Dutch Clinical Trial Registration no: NTR1361.

KEYWORDS: ERCP; cost comparison; pancreatic cancer; randomized trial

PMID: 25790742

### Reply to "Can we avoid rectus abdominis muscle atrophy and midline shift after colostomy creation?"

Timmermans L1, Deerenberg EB1, van Dijk SM1, **Lamme B2**, Koning AH3, Kleinrensink GJ4, Jeekel J4, Lange JF1.

Surgery. 2015 Jan;157(1):179-80. doi: 10.1016/j.surg.2014.09.021.

We read with interest the letter to the editor by Stephenson et al regarding our article "Abdominal rectus muscle atrophy and midline shift after colostomy creation."

1. Any attempt to decrease the risk of parastomal herniation should be applauded, because its incidence of greater than 50% remains unacceptably high. Transrectus vs pararectal stoma placement has been subject to discussion for quite some time, is retrospective in nature, and thus the level of evidence is low. The most recent Cochrane review concludes that the poor quality of the included evidence did not allow a robust conclusion.
2. In addition, no difference could be discovered after we pooled all studies, which comprised a total number of 761 patients. Furthermore, the authors describe in their letter that they could not observe a midline shift in their trial; however, as we mention in our study, we could only determine the true midline by using the I-Space, a CAVE-like virtual reality system and V-scope software, so we are interested as to how the authors determined a midline without these tools. Applying new techniques to prevent this complication seems highly relevant, because the impact of parastomal hernia on the quality of life of patients should not be underestimated (unpublished results).
3. Placement of the stoma lateral to the rectus muscles could possibly decrease the rate of parastomal hernia, as is suggested by the retrospective study of Stephenson et al.
4. The intercostal nerves are less segmented lateral to the stoma and could be easier to detect and preserve. Randomized, controlled trials, however, are needed to evaluate the effect of this technique. A possible technique for parastomal hernia prevention is the use of primary mesh augmentation. A meta-analysis focusing on primary mesh augmentation showed a decrease in parastomal hernia with a risk ratio of 0.23. Interestingly, no mesh infections were reported in any of the randomized controlled trials,
5. but the use of prosthetic material in potentially contaminated areas are still a subject of debate. Possibly, the long-term results of the PREVENT trial could give us more information regarding this prevention method.

PMID: 25482472

**Surveillance in patients with long-segment Barrett's oesophagus: a cost-effectiveness analysis.**

Kastelein F1, van Olphen S2, Steyerberg EW3, Sikkema M4, Spaander MC1, Looman CW3, Kuipers EJ1, Siersema PD4, Bruno MJ1, de Bekker-Grob EW3; **ProBar-study group.** Biermann, Geldof H, van der Valk H, ter Borg PC, Giard RW, Felt RJ, Meijer GA, **Alderliesten J**, Heinhuis R, ter Borg F, Arends JW, Kolkman JJ, van Baarlen J, Tan TG, den Hartog B, van Tilburg AJ, Engels LG, Vos W, Peters FT, Karrenbeld A, Schenk BE, Moll F, Loffeld R, Flens M, van Roermund H, lockefeer F. Gut. 2015 Jun;64(6):864-71. doi: 10.1136/gutjnl-2014-307197. Epub 2014 Jul 18.

**OBJECTIVE:** Surveillance is recommended for Barrett's oesophagus (BO) to detect early oesophageal adenocarcinoma (OAC). The aim of this study was to evaluate the cost-effectiveness of surveillance.

**DESIGN:** We included 714 patients with long-segment BO in a multicentre prospective cohort study and used a multistate Markov model to calculate progression rates from no dysplasia (ND) to low-grade dysplasia (LGD), high-grade dysplasia (HGD) and OAC. Progression rates were incorporated in a decision-analytic model, including costs and quality of life data. We evaluated different surveillance intervals for ND and LGD, endoscopic mucosal resection (EMR), radiofrequency ablation (RFA) and oesophagectomy for HGD or early OAC and oesophagectomy for advanced OAC. The incremental cost-effectiveness ratio (ICER) was calculated in costs per quality-adjusted life-year (QALY).

**RESULTS:** The annual progression rate was 2% for ND to LGD, 4% for LGD to HGD or early OAC and 25% for HGD or early OAC to advanced OAC. Surveillance every 5 or 4 years with RFA for HGD or early OAC and oesophagectomy for advanced OAC had ICERs of €5.283 and €62.619 per QALY for ND. Surveillance every five to one year had ICERs of €4.922, €30.067, €32.531, €41.499 and €75.601 per QALY for LGD. EMR prior to RFA was slightly more expensive, but important for tumour staging.

**CONCLUSIONS:** Based on a Dutch healthcare perspective and assuming a willingness-to-pay threshold of €35.000 per QALY, surveillance with EMR and RFA for HGD or early OAC, and oesophagectomy for advanced OAC is cost-effective every 5 years for ND and every 3 years for LGD.

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**KEYWORDS:** BARRETT'S CARCINOMA; BARRETT'S METAPLASIA; BARRETT'S OESOPHAGUS; COST-EFFECTIVENESS; OESOPHAGEAL CANCER

PMID: 25037191

# Medische Microbiologie

## **Dysbiosis of upper respiratory tract microbiota in elderly pneumonia patients.**

de Steenhuijsen Piters WA1, **Huijskens EG2**, Wyllie AL1, Biesbroek G1, van den Bergh MR3, Veenhoven RH4, Wang X1, Trzciński K1, Bonten MJ5, Rossen JW6, Sanders EA1, Bogaert D1. ISME J. 2016 Jan;10(1):97-108. doi: 10.1038/ismej.2015.99. Epub 2015 Jul 7.

Bacterial pneumonia is a major cause of morbidity and mortality in elderly. We hypothesize that dysbiosis between regular residents of the upper respiratory tract (URT) microbiome, that is balance between commensals and potential pathogens, is involved in pathogen overgrowth and consequently disease. We compared oropharyngeal microbiota of elderly pneumonia patients (n=100) with healthy elderly (n=91) by 16S-rRNA-based sequencing and verified our findings in young adult pneumonia patients (n=27) and young healthy adults (n=187). Microbiota profiles differed significantly between elderly pneumonia patients and healthy elderly (PERMANOVA,  $P < 0.0005$ ). Highly similar differences were observed between microbiota profiles of young adult pneumonia patients and their healthy controls. Clustering resulted in 11 (sub)clusters including 95% (386/405) of samples. We observed three microbiota profiles strongly associated with pneumonia ( $P < 0.05$ ) and either dominated by lactobacilli (n=11), *Rothia* (n=51) or *Streptococcus (pseudo)pneumoniae* (n=42). In contrast, three other microbiota clusters (in total n=183) were correlated with health ( $P < 0.05$ ) and were all characterized by more diverse profiles containing higher abundances of especially *Prevotella melaninogenica*, *Veillonella* and *Leptotrichia*. For the remaining clusters (n=99), the association with health or disease was less clear. A decision tree model based on the relative abundance of five bacterial community members in URT microbiota showed high specificity of 95% and sensitivity of 84% (89% and 73%, respectively, after cross-validation) for differentiating pneumonia patients from healthy individuals. These results suggest that pneumonia in elderly and young adults is associated with dysbiosis of the URT microbiome with bacterial overgrowth of single species and absence of distinct anaerobic bacteria. Whether the observed microbiome changes are a cause or a consequence of the development of pneumonia or merely coincide with disease status remains a question for future research.

PMID: 26151645

## **Evaluation of different real time PCRs for the detection of *Pneumocystis jirovecii* DNA in formalin-fixed paraffin-embedded bronchoalveolar lavage samples.**

de Leeuw BH1, Voskuil WS2, **Maraha B3**, van der Zee A4, **Westenend PJ5**, Kusters JG2. Exp Mol Pathol. 2015 Jun;98(3):390-2. doi: 10.1016/j.yexmp.2015.03.021. Epub 2015 Mar 13.

The presence of *Pneumocystis jirovecii* in fresh clinical materials can be detected by PCR with high sensitivity and is thus preferred over microscopic methods. However, fresh materials are not always available, and on formalin-fixed paraffin-embedded materials, PCR may result in reduced detection rates. In this study the diagnostic sensitivity of *P. jirovecii* real time PCR on DNA isolated from fresh bronchoalveolar lavage (BAL) samples versus that from matched FFPE derived DNA is analyzed. Our results indicate that when targeting a small DNA fragment *P.*

jirovecii PCR can be performed on FFPE BAL samples with acceptable sensitivity (up to 83.3%). This is considerably higher than the 33.3% positives observed by classical staining of these samples.

PMID: 25779023

### **Evaluation of Patients with Community-Acquired Pneumonia Caused by Zoonotic Pathogens in an Area with a High Density of Animal Farms.**

Huijskens EG1,2, Smit LA3, Rossen JW2,4, Heederik D3, Koopmans M5,6.

Zoonoses Public Health. 2015 Jul 27. doi: 10.1111/zph.12218. [Epub ahead of print]

Intensive animal farming could potentially lead to outbreaks of infectious diseases. Clinicians are at the forefront of detecting unusual diseases, but the lack of specificity of zoonotic disease symptoms makes this a challenging task. We evaluated patients with community-acquired pneumonia (CAP) with known and unknown aetiology in an area with a high livestock density and a potential association with animal farms in the proximity. Between 2008 and 2009, a period coinciding with a large Q fever outbreak in the Netherlands, patients with CAP were tested for the presence of possible respiratory pathogens. The presence and number of farm animals within 1 km of the patients' home address were assessed using geographic information system (GIS) and were compared between cases and age-matched control subjects. Of 408 patients with CAP, pathogens were detected in 275 (67.4%) patients. The presence of sheep and the number of goats were associated with CAP caused by *Coxiella burnetii* in a multiple logistic regression model ( $P < 0.05$ ). CAP with unknown aetiology was not associated with the presence of animal farms ( $P > 0.10$ ). The use of GIS in combination with aetiology of CAP could be potentially used to target diagnostics and to identify outbreaks of rare zoonotic disease. **KEYWORDS:** *Coxiella burnetii* ; Zoonosis; community-acquired pneumonia; geographic information system; respiratory pathogens

PMID: 26214299

### **Gram-positive cocci in Dutch ICUs with and without selective decontamination of the oropharyngeal and digestive tract: a retrospective database analysis.**

van der Bij AK1, Frenz D2, Bonten MJ3; ISIS-AR Study Group.

Collaborators (50):

Stuart JW, van Hees BC, Vijfhuizen J, Wintermans RG, der Kuil WA, Alblas J, van der Bij AK, Frenz D, van Heereveld J, Hertroys R, Leenstra T, Monen JC, Woudt SH, de Greeff SC, van Keulen PH, Kluytmans JA, Mattsson EE, Sebens FW, Frenay HM, **Maraha B**, Halaby T, Versteeg D, Hendrix R, Schellekens JF, Diederens BM, de Brauwier EI, Stals FS, Bakker LJ, Dorigo-Zetsma JW, van Zeijl JH, Bernardts AT, de Jongh BM, Vlaminckx BJ, Horrevorts A, Kuipers S, Wintermans RG, Moffie B, Brimicombe RW, Jansen CL, Renders NH, Hendrickx BG, Buiting AG, Thijsen SF, Deege MP, Frakking FN, Tjhie HT, van Zwet AA, Voorn GP, Ruijs GJ, Wolfhagen MJ.

J Antimicrob Chemother. 2015 Dec 11. pii: dkv396. [Epub ahead of print]

**OBJECTIVES:** The objective of this study was to determine time trends in the rate of Gram-positive cocci in 42 Dutch ICUs that continuously used or did not use selective oropharyngeal decontamination (SOD) or selective decontamination of the digestive tract (SDD) and ICUs that introduced SOD/SDD.

**METHODS:** The Dutch Surveillance System on Antibiotic Resistance was used to determine monthly rates of *Staphylococcus aureus*, *Enterococcus faecalis* and *Enterococcus faecium* isolates, including resistant phenotypes, in blood and respiratory tract specimens from 2008 to 2013. Per patient, the last isolate per species per month was selected, and cumulative rates per 100 beds per month were determined. Time trends were analysed by multilevel Poisson regression.

**RESULTS:** Eighteen ICUs used SOD/SDD (1296 months), 13 did not use SOD/SDD (936 months) and 11 introduced SOD/SDD (373 months before and 419 months after introduction). There was no significant increase in the rate of Gram-positive cocci in ICUs that used SOD/SDD. Introduction of SOD/SDD was associated with increased rates of *S. aureus* ( $\beta=0.018$ , 95% CI 0.006-0.030) and *E. faecalis* isolates ( $\beta=0.028$ , 95% CI 0.006-0.051) in respiratory tract specimens. Numbers of resistant phenotypes remained low, and an observed increase in *E. faecium* isolates ( $\beta=0.033$ , 95% CI 0.012-0.054), 97% of which were resistant to ampicillin, in the absence of SOD/SDD disappeared after the introduction of SOD/SDD.

**CONCLUSIONS:** In ICUs with a low endemicity of resistance, introduction of SOD/SDD was associated with increased rates of *S. aureus* and *E. faecalis* isolates, but not with resistant phenotypes. Continuous 5 year use of SOD/SDD was not associated with increased isolation of Gram-positive cocci. © The Author 2015. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.

PMID: 26661393

### Infectious diseases linked to cross-contamination of flexible endoscopes.

**N Kenters<sup>1\*</sup>, EGW Huijskens<sup>2</sup>, C Meier<sup>3</sup> and A Voss<sup>4</sup>**

Endosc Int Open. 2015 Aug;3(4):E259-65. doi: 10.1055/s-0034-1392099.

Flexible endoscopes are widely used to examine, diagnose, and treat medical disorders. While the risk of endoscopy-related transmission of infection is estimated to be very low, more health care-associated infections are related to contaminated endoscopes than to any other medical device. Flexible endoscopes can get highly contaminated with microorganisms, secretions and blood during use. The narrow lumens and multiple internal channels make the cleaning of flexible endoscopes a complex and difficult task. Despite the availability of international, national and local endoscope reprocessing guidelines, contamination and transmission of microorganisms continue to occur. These transmissions are mostly related to the use of defective equipment, endoscope reprocessing failures, and noncompliance with recommended guidelines. This article presents an overview of publications about case reports and outbreaks related to contamination of flexible endoscopes.

PMID: 26355428

### Trends in Expanded-Spectrum Cephalosporin-Resistant *Escherichia coli* and *Klebsiella pneumoniae* among Dutch Clinical Isolates, from 2008 to 2012.

van der Steen M1, Leenstra T2, Kluytmans JA3, van der Bij AK4; **ISIS-AR study group.**

Collaborators: ...Frénay, HM, **Maraha, B...**

PLoS One. 2015 Sep 18;10(9):e0138088. doi: 10.1371/journal.pone.0138088.

We investigated time trends in extended-spectrum cephalosporin-resistant *Escherichia coli* and *Klebsiella pneumoniae* isolates from different patient settings in The Netherlands from

2008-2012. *E. coli* and *K. pneumoniae* isolates from blood and urine samples of patients  $\geq 18$  years were selected from the Dutch Infectious Disease Surveillance System-Antimicrobial Resistance (ISIS-AR) database. We used multivariable Poisson regression to study the rate per year of blood stream infections by susceptible and resistant isolates, and generalized estimating equation (GEE) log-binomial regression for trends in the proportion of extended-spectrum cephalosporin-resistant isolates. Susceptibility data of 197,513 *E. coli* and 38,244 *K. pneumoniae* isolates were included. The proportion of extended-spectrum cephalosporin-resistant *E. coli* and *K. pneumoniae* isolates from urine and blood samples increased in all patient settings, except for *K. pneumoniae* isolates from patients admitted to intensive care units. For *K. pneumoniae*, there was a different time trend between various patient groups ( $p < 0.01$ ), with a significantly higher increase in extended-spectrum cephalosporin-resistant isolates from patients attending a general practitioner than in isolates from hospitalized patients. For *E. coli*, the increasing time trends did not differ among different patient groups. This nationwide study shows a general increase in extended-spectrum cephalosporin-resistant *E. coli* and *K. pneumoniae* isolates. However, differences in trends between *E. coli* and *K. pneumoniae* underline the importance of *E. coli* as a community-pathogen and its subsequent influence on hospital resistance level, while for *K. pneumoniae* the level of resistance within the hospital seems less influenced by the resistance trends in the community.

PMID: 26381746

## Diagnostic yield and accuracy of CT angiography, MR angiography, and digital subtraction angiography for detection of macrovascular causes of intracerebral haemorrhage: prospective, multicentre cohort study.

van Asch CJ1, Velthuis BK2, Rinkel GJ3, Algra A4, de Kort GA2, Witkamp TD2, de Ridder JC3, van Nieuwenhuizen KM3, de Leeuw FE5, Schonewille WJ6, de Kort PL7, Dippel DW8, Raaymakers TW9, Hofmeijer J10, Wermer MJ11, **Kerckhoff H12**, Jellema K13, Bronner IM14, Remmers MJ15, Bienfait HP16, Witjes RJ17, Greving JP18, Klijn CJ19; DIAGRAM Investigators.

BMJ. 2015 Nov 9;351:h5762. doi: 10.1136/bmj.h5762.

**STUDY QUESTION:** What are the diagnostic yield and accuracy of early computed tomography (CT) angiography followed by magnetic resonance imaging/angiography (MRI/MRA) and digital subtraction angiography (DSA) in patients with non-traumatic intracerebral haemorrhage?

**METHODS:** This prospective diagnostic study enrolled 298 adults (18-70 years) treated in 22 hospitals in the Netherlands over six years. CT angiography was performed within seven days of haemorrhage. If the result was negative, MRI/MRA was performed four to eight weeks later. DSA was performed when the CT angiography or MRI/MRA results were inconclusive or negative. The main outcome was a macrovascular cause, including arteriovenous malformation, aneurysm, dural arteriovenous fistula, and cavernoma. Three blinded neuroradiologists independently evaluated the images for macrovascular causes of haemorrhage. The reference standard was the best available evidence from all findings during one year's follow-up.

**STUDY ANSWER AND LIMITATIONS:** A macrovascular cause was identified in 69 patients (23%). 291 patients (98%) underwent CT angiography; 214 with a negative result underwent additional MRI/MRA and 97 with a negative result for both CT angiography and MRI/MRA underwent DSA. Early CT angiography detected 51 macrovascular causes (yield 17%, 95% confidence interval 13% to 22%). CT angiography with MRI/MRA identified two additional macrovascular causes (18%, 14% to 23%) and these modalities combined with DSA another 15 (23%, 18% to 28%). This last extensive strategy failed to detect a cavernoma, which was identified on MRI during follow-up (reference strategy). The positive predictive value of CT angiography was 72% (60% to 82%), of additional MRI/MRA was 35% (14% to 62%), and of additional DSA was 100% (75% to 100%). None of the patients experienced complications with CT angiography or MRI/MRA; 0.6% of patients who underwent DSA experienced permanent sequelae. Not all patients with negative CT angiography and MRI/MRA results underwent DSA. Although the previous probability of finding a macrovascular cause was lower in patients who did not undergo DSA, some small arteriovenous malformations or dural arteriovenous fistulas may have been missed.

**WHAT THIS STUDY ADDS:** CT angiography is an appropriate initial investigation to detect macrovascular causes of non-traumatic intracerebral haemorrhage, but accuracy is modest. Additional MRI/MRA may find cavernomas or alternative diagnoses, but DSA is needed to diagnose macrovascular causes undetected by CT angiography or MRI/MRA.

**FUNDING, COMPETING INTERESTS, DATA SHARING:** Dutch Heart Foundation and The Netherlands Organisation for Health Research and

Development, ZonMw. The authors have no competing interests. Direct requests for additional data to the corresponding author. © van Asch et al 2015.

PMID: 26553142

### **Intravenous immunoglobulin response in treatment-naïve chronic inflammatory demyelinating polyradiculoneuropathy.**

**Kuitwaard K1**, Hahn AF2, Vermeulen M3, Venance SL2, van Doorn PA4.

J Neurol Neurosurg Psychiatry. 2015 Dec;86(12):1331-6. doi: 10.1136/jnnp-2014-309042.

Epub 2014 Dec 16.

**OBJECTIVE:** There is no consensus on which treatment should be used preferentially in individual patients with chronic inflammatory demyelinating polyneuropathy (CIDP). Patients unlikely to respond to intravenous immunoglobulin (IVIg) could be prescribed corticosteroids first to avoid high cost and a delayed treatment response. We investigated which factors determined a response to IVIg.

**METHODS:** Treatment-naïve patients with CIDP initially treated with at least one full course of IVIg (2 g/kg) at one of two neuromuscular disease centres were included. Patients fulfilled the European Federation of Neurological Societies/Peripheral Nerve Society clinical criteria for CIDP. Significant improvement following IVIg was defined as an improvement ( $\geq 1$  grade) on the modified Rankin scale. Difference in weakness between arms and legs was defined as  $\geq 2$  grades on the Medical Research Council scale between ankle dorsiflexion and wrist extension. Clinical predictors with a p value  $< 0.15$  in univariate analysis were analysed in multivariate logistic regression.

**RESULTS:** Of a total of 281 patients, 214 patients (76%) improved. In univariate analysis, the presence of pain, other autoimmune disease, difference in weakness between arms and legs, and a myelin-associated glycoprotein negative IgM monoclonal gammopathy of undetermined significance were associated with no response to IVIg. In multivariate analysis no pain ( $p=0.018$ ) and no difference in weakness between arms and legs ( $p=0.048$ ) were independently associated with IVIg response. Of IVIg non-responders, 66% improved with plasma exchange and 58% with corticosteroids.

**CONCLUSIONS:** IVIg is a very effective first-line treatment. Patients with CIDP presenting with pain or a difference in weakness between arms and legs are less likely to respond to IVIg. Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to <http://group.bmj.com/group/rights-licensing/permissions>.

**KEYWORDS:** CLINICAL NEUROLOGY; GUILLAIN-BARRE SYNDROME; NEUROIMMUNOLOGY; NEUROMUSCULAR; NEUROPATHY

PMID: 25515502

### **Pathologically confirmed autoimmune encephalitis in suspected Creutzfeldt-Jakob disease.**

Maat P1, **de Beukelaar JW1**, Jansen C1, Schuur M1, van Duijn CM1, van Coevorden MH1, de Graaff E1, Titulaer M1, Rozemuller AJ1, Sillevs Smitt P1.

Neurol Neuroimmunol Neuroinflamm. 2015 Nov 12;2(6):e178. eCollection 2015.

**OBJECTIVE:** To determine the clinical features and presence in CSF of antineuronal antibodies in patients with pathologically proven autoimmune encephalitis derived from a cohort of

patients with suspected Creutzfeldt-Jakob disease (CJD).

**METHODS:** The Dutch Surveillance Centre for Prion Diseases performed 384 autopsies on patients with suspected CJD over a 14-year period (1998-2011). Clinical information was collected from treating physicians. Antineuronal antibodies were tested in CSF obtained postmortem by immunohistochemistry on fresh frozen rat brain sections, by Luminex assay for the presence of well-characterized onconeural antibodies, and by cell-based assays for antibodies against NMDAR, GABABR1/2, GABAAR GLUR1/2, LGI1, Caspr2, and DPPX.

**RESULTS:** In 203 patients, a diagnosis of definite CJD was made, while in 181 a variety of other conditions were diagnosed, mainly neurodegenerative. In 22 of these 181, the neuropathologist diagnosed autoimmune encephalitis. One patient was excluded because of lack of clinical information. Inflammatory infiltrates were predominantly perivascular and consisted mainly of T cells. The predominant locations were basal ganglia and thalamus (90%) and temporal lobes and hippocampus (81%). In 6 patients (29%), antineuronal antibodies were detected in postmortem CSF, directed against Hu, NMDAR, GABABR1/2, Caspr2, and an unidentified synaptic antigen in 2. The most frequent symptoms were dementia (90%), gait disturbance (86%), cerebellar signs (67%), and neuropsychiatric symptoms (67%). Immunopathologic and clinical findings did not differ between autoantibody-negative patients and patients with antineuronal antibodies.

**CONCLUSIONS:** It is important to consider immune-mediated disorders in the differential diagnosis of rapidly progressive neurologic deficits.

PMID: 26601117

### **The Preventive Antibiotics in Stroke Study (PASS): a pragmatic randomised open-label masked endpoint clinical trial**

Westendorp WF1, Vermeij JD1, **Zock E2**, Hooijenga IJ1, Kruijt ND3, Bosboom HJ4, Kwa VI4, Weisfelt M5, Remmers MJ6, Ten Houten R7, Schreuder AH8, Vermeer SE9, van Dijk EJ10, Dippel DW11, Dijkgraaf MG12, Spanjaard L13, Vermeulen M1, van der Poll T14, Prins JM14, Vermeij FH15, Roos YB1, **Kleyweg RP2**, **Kerkhoff H2**, Brouwer MC1, Zwinderman AH16, van de Beek D17, Nederkoorn PJ1; for the PASS investigators.

Lancet. 2015 Apr 18;385(9977):1519-26. doi: 10.1016/S0140-6736(14)62456-9. Epub 2015 Jan 20.

**BACKGROUND:** In adults with acute stroke, infections occur commonly and are associated with an unfavourable functional outcome. In the Preventive Antibiotics in Stroke Study (PASS) we aimed to establish whether or not preventive antimicrobial therapy with a third-generation cephalosporin, ceftriaxone, improves functional outcome in patients with acute stroke.

**METHODS:** In this multicentre, randomised, open-label trial with masked endpoint assessment, patients with acute stroke were randomly assigned to intravenous ceftriaxone at a dose of 2 g, given every 24 h intravenously for 4 days, in addition to stroke unit care, or standard stroke unit care without preventive antimicrobial therapy; assignments were made within 24 h after symptom onset. The primary endpoint was functional outcome at 3 months, defined according to the modified Rankin Scale and analysed by intention to treat. The primary analysis was by ordinal regression of the primary outcome. Secondary outcomes included death, infection rates, antimicrobial use, and length of hospital stay. Participants and caregivers were aware of treatment allocation but assessors of outcome were masked to group assignment.

This trial is registered with controlled-trials.com, number ISRCTN66140176.

**FINDINGS:** Between July 6, 2010, and March 23, 2014, a total of 2550 patients from 30 sites in the Netherlands, including academic and non-academic medical centres, were randomly

assigned to the two treatment groups: 1275 patients to ceftriaxone and 1275 patients to standard treatment (control group). 12 patients (seven in the ceftriaxone group and five in the control group) withdrew consent immediately after randomisation, leaving 2538 patients available for the intention-to-treat-analysis (1268 in the ceftriaxone group and 1270 in the control group). 2514 (99%) of 2538 patients (1257 in each group) completed 3-month follow-up. Preventive ceftriaxone did not affect the distribution of functional outcome scores on the modified Rankin Scale at 3 months (adjusted common odds ratio 0.95 [95% CI 0.82-1.09],  $p=0.46$ ). Preventive ceftriaxone did not result in an increased occurrence of adverse events. Overgrowth infection with *Clostridium difficile* occurred in two patients (<1%) in the ceftriaxone group and none in the control group.

**INTERPRETATION:** Preventive ceftriaxone does not improve functional outcome at 3 months in adults with acute stroke. The results of our trial do not support the use of preventive antibiotics in adults with acute stroke.

**FUNDING:** Netherlands Organization for Health Research and Development, Netherlands Heart Foundation, and the European Research Council.

*PMID: 25612858*

# Nucleaire Geneeskunde

**[A man with an abnormal PET-CT scan]. Een man met een afwijkende PET-CT-scan**  
**Meulman TJ1, Ho-Han SH, Hendriksz TR.**

Ned Tijdschr Geneeskd. 2015;159(0):A9343.

A 65-year-old patient with rectal carcinoma underwent an 18FDG PET-CT scan. The scan showed nodular foci of 18FDG uptake against the ventral abdominal wall, possibly carcinomatous peritonitis. These abnormalities were caused by a foreign body reaction to a mesh that was placed five months earlier because of an umbilical hernia repair.

PMID: 26507066

# Ouderengeneeskunde

## [Diagnostic imaging in dementia: use of imaging modalities in Dutch memory clinics].

**Gardeniers M1, Wattjes MP2, Meulen EF3, Barkhof F2, Bakker J4.**

Tijdschr Gerontol Geriatr. 2015 Nov 2. [Epub ahead of print]

**PURPOSE:** To evaluate the use of MRI and CT in the diagnostic work-up of dementia in Dutch memory clinics, and to analyse the rationale for choosing each modality.

**MATERIALS AND METHODS:** A digital survey was sent by e-mail to all medical specialists (n=235) working at a memory clinic in the Netherlands.

**RESULTS:** The survey was completed by 64% (151). 85% of the respondents were geriatricians, 13% neurologists and 2% other, working at a total of 69 clinics. 40% variably orders CT or MRI, 37% orders MRI, 19% CT, and 4% CT plus MRI. Primary factors influencing this choice are: MRI contraindications, physical limitations, age, vascular or oncological medical history, and waiting time. With CT, 87% indicates information is lacking: vascular disease/white matter lesions, (hippocampal) atrophy, and specific pathologies (metastases, amyloid angiopathy). Furthermore, respondents prefer MRI because they can assess the images more easily themselves. Only 50% of respondents indicate that CT protocol dictates coronal reconstructions. Additionally, these reconstructions are not provided consistently. Rating-scales are used to describe images in 5%. In 75% assessment is not uniform.

**CONCLUSION:** MRI is preferred over CT in diagnostic imaging of dementia, in accordance with existing guidelines. However, these guidelines are mostly out-dated and modern multislice CT potential is relatively unknown among geriatricians. In memory clinics, multislice CT could offer a well suitable imaging alternative, but only if multiplanar reconstructions are performed consistently. Furthermore, radiology reports need to be improved by using more standardized assessment.

PMID: 26525706

## 9B.09: IDENTIFICATION OF MARKERS PREDICTIVE FOR MALIGNANT BEHAVIOR OF PHEOCHROMOCYTOMAS AND PARAGANGLIOMAS.

Evenepoel L1, **Van Nederveen FH**, Oudijk L, Papathomas TG, Restuccia DF, Belt EJ, Franssen GJ, Feelders RA, Van Eeden S, Timmers H, De Herder WW, Aydin S, Vikkula M, De Krijger RR, Dinjens WN, Persu A, Korpershoek E.

J Hypertens. 2015 Jun;33 Suppl 1:e122. doi: 10.1097/01.hjh.0000467681.47178.d5.

**OBJECTIVE:** Pheochromocytomas and paragangliomas (PPGL) are relatively rare and mostly benign tumours. Approximately 10% of PPGL are malignant, as defined by the presence of metastases, i.e chromaffin tissue at a location that usually does not contain chromaffin cells. However, up to 35% of tumours in patients carrying an SDHB mutation appears to be malignant. Nowadays, no reliable marker allows to predict whether a PPGL is, or will become malignant. In addition, there are no curative treatments if metastases occur. The aim of the present study was to identify genetic markers allowing to distinguish benign from malignant tumours.

**DESIGN AND METHOD:** An mRNA expression array was performed on benign and malignant PPGL. The genes showing a different expression between the benign and malignant tumours were selected to be confirmed and validated by qRT-PCR. Finally, the remaining genes were stained by immunohistochemistry on Tissue MicroArray including a large series of PPGL.

**RESULTS:** Forty benign and 12 malignant PPGL were investigated for differences in mRNA expression with Affymetrix arrays. Expression data were normalized according to Affymetrix recommendations. Then, using Pomelo II (<http://pomelo2.bioinfo.cnio.es/>), a Limma t-test was performed, to assess which genes were differentially expressed between benign and malignant PPGL. First, a non-clustered analysis was performed and 10 genes with a False Discovery Rate (FDR) below 0.05 and a relative overexpression ratio of at least 4 were found, including Interleukin 13 Receptor alpha 2 (IL13RA2) and Monooxygenase DBH-like 1 (MOXD1). Secondly, a supervised cluster analysis was performed (based on HIF target genes), resulting in 2 groups, which were both investigated for differences in mRNA expression between benign and malignant tumours. Five genes showed an FDR below 0.01 and were overexpressed in malignant tumours with a ratio higher than 4, including Contactin 4 (CNTN4), Iroquois Homeobox 3 (IRX3), and Sulfatase 2 (SULF2). These genes were further investigated using qRT-PCR, and immunohistochemistry on Tissue Micro Array including 91 benign and 12 malignant PPGL. **CONCLUSIONS:** Significant overexpression of Contactin 4 was shown in malignant compared to benign tumours, and may therefore contribute to distinguish malignant from benign PPGL.

PMID: 26102717

### [A boy with a chronic swelling of the upper lip].

**van der Bent SA1, Kuizinga MC, van der Velden JJ.**

Ned Tijdschr Geneeskd. 2015;159(0):A9103.

A 14-year-old boy developed a chronic painless swelling of the upper lip. Histology of a skin

biopsy showed non-necrotizing tuberculoid granulomas. The diagnosis cheilitis granulomatosa was made.

PMID: 26230346 [PubMed - in process]

### **An International Ki67 Reproducibility Study in Adrenal Cortical Carcinoma.**

Papathomas TG1, Pucci E, Giordano TJ, Lu H, Duregon E, Volante M, Papotti M, Lloyd RV, Tischler AS, **van Nederveen FH**, Nose V, Erickson L, Mete O, Asa SL, Turchini J, Gill AJ, Matias-Guiu X, Skordilis K, Stephenson TJ, Tissier F, Feelders RA, Smid M, Nigg A, Korpershoek E, van der Spek PJ, Dinjens WN, Stubbs AP, de Krijger RR.

Am J Surg Pathol. 2015 Dec 17. [Epub ahead of print]

Despite the established role of Ki67 labeling index in prognostic stratification of adrenocortical carcinomas and its recent integration into treatment flow charts, the reproducibility of the assessment method has not been determined. The aim of this study was to investigate interobserver variability among endocrine pathologists using a web-based virtual microscopy approach. Ki67-stained slides of 76 adrenocortical carcinomas were analyzed independently by 14 observers, each according to their method of preference including eyeballing, formal manual counting, and digital image analysis. The interobserver variation was statistically significant ( $P < 0.001$ ) in the absence of any correlation between the various methods. Subsequently, 61 static images were distributed among 15 observers who were instructed to follow a category-based scoring approach. Low levels of interobserver ( $F = 6.99$ ;  $F_{crit} = 1.70$ ;  $P < 0.001$ ) as well as intraobserver concordance ( $n = 11$ ; Cohen  $\kappa$  ranging from  $-0.057$  to  $0.361$ ) were detected. To improve harmonization of Ki67 analysis, we tested the utility of an open-source Galaxy virtual machine application, namely Automated Selection of Hotspots, in 61 virtual slides. The software-provided Ki67 values were validated by digital image analysis in identical images, displaying a strong correlation of  $0.96$  ( $P < 0.0001$ ) and dividing the cases into 3 classes (cutoffs of 0%-15%-30% and/or 0%-10%-20%) with significantly different overall survivals ( $P < 0.05$ ). We conclude that current practices in Ki67 scoring assessment vary greatly, and interobserver variation sets particular limitations to its clinical utility, especially around clinically relevant cutoff values. Novel digital microscopy-enabled methods could provide critical aid in reducing variation, increasing reproducibility, and improving reliability in the clinical setting.

PMID: 26685085

### **Complex MAX rearrangement in a family with malignant pheochromocytoma, renal oncocytoma and erythrocytosis.**

Korpershoek E1, Koffy D1, Eussen BH2, Oudijk L1, Papathomas TG1,3, **van Nederveen FH4**, Belt EJ5, Franssen GJ5, Restuccia DF1, Krol NM1, van der Luijt RB6, Feelders RA7, Oldenburg RA2, van Ijcken WF8, de Klein A2, de Herder WW7, de Krijger RR1,9, Dinjens WN1.

J Clin Endocrinol Metab. 2015 Dec 15;jc20152592. [Epub ahead of print]

CONTEXT: Familial pheochromocytoma (PCC) has been associated with germline mutations in 16 genes. Here we investigated three siblings presenting with bilateral pheochromocytomas. In addition, the index patient also exhibited renal oncocytoma and erythrocytosis, whereas the second sibling presented with a lymph node metastasis.

DESIGN: First, SNP array and exome sequencing were performed on germline and PCC-derived DNA to identify genomic alterations in the index patient. Second, alterations were confirmed and validated by Sanger sequencing, analyzed by (multiplexed) PCR to determine loss of the

wild-type allele, and investigated by immunohistochemistry in the tumors of the three siblings. RESULTS: The index patient's germline DNA revealed a large complex genomic alteration encompassing the intragenic and promoter regions of Myc-Associated Factor X (MAX) and alpha-(1,6)-fucosyltransferase (FUT8). In all three siblings the MAX alteration was confirmed and loss of the wild type MAX and FUT8 alleles was demonstrated in all tumors. Uniparental disomy of chromosome 14q, previously demonstrated as a hallmark for MAX-related PCC, was shown in the index patient's PCC by SNP-array. Loss of MAX and FUT8 protein expression was demonstrated by immunohistochemistry in the tumors from the three siblings.

CONCLUSIONS: Our results indicate that large genomic deletions of MAX should be considered in familial and bilateral PCC with prior negative testing for gene mutations. In addition, our results confirm that MAX is a tumor suppressor gene for renal oncocytomas.

PMID: 26670126

### Evaluation of different real time PCRs for the detection of *Pneumocystis jirovecii* DNA in formalin-fixed paraffin-embedded bronchoalveolar lavage samples.

de Leeuw BH1, Voskuil WS2, Maraha B3, van der Zee A4, Westenend PJ5, Kusters JG2.

Exp Mol Pathol. 2015 Jun;98(3):390-2. doi: 10.1016/j.yexmp.2015.03.021. Epub 2015 Mar 13.

The presence of *Pneumocystis jirovecii* in fresh clinical materials can be detected by PCR with high sensitivity and is thus preferred over microscopic methods. However, fresh materials are not always available, and on formalin-fixed paraffin-embedded materials, PCR may result in reduced detection rates. In this study the diagnostic sensitivity of *P. jirovecii* real time PCR on DNA isolated from fresh bronchoalveolar lavage (BAL) samples versus that from matched FFPE derived DNA is analyzed. Our results indicate that when targeting a small DNA fragment *P. jirovecii* PCR can be performed on FFPE BAL samples with acceptable sensitivity (up to 83.3%). This is considerably higher than the 33.3% positives observed by classical staining of these samples.

PMID: 25779023

### [Guideline thyroid cancer including diagnostics of the nodule]. [Article in Dutch]

Links TP1, de Heide LJ, Janssen M, van Nederveen FH, van der Lugt A, Vriens MR, Smit JW. Ned Tijdschr Geneesk. 2015;159:A9413.

- Thyroid cancer is comparatively rare. Thyroid nodules, on the other hand, are frequently diagnosed as a result of increasing use of diagnostic imaging.- Cytological investigation of small nodules that have been found by chance often reveals micropapillary carcinoma that is probably not clinically relevant.- The new guideline 'Thyroid cancer' advises that cytological investigation of these non-palpable, incidentally discovered thyroid nodules should only be performed on indication.- The standard treatment for patients with papillary or follicular thyroid cancer consists of thyroidectomy followed by, if indicated, lymph-node dissection, ablation therapy with radioactive iodine and TSH-suppression. The extent of this treatment is determined on the basis of known prognostic factors and the results of initial treatment.- Targeted systemic therapy is available for patients with metastatic progressive disease.- There is more focus on the effects of short- and long-term treatment, in order to optimise quality of life.

PMID: 26556492

### **Impact of Age at Primary Breast Cancer on Contralateral Breast Cancer Risk in BRCA1/2 Mutation Carriers.**

van den Broek AJ1, van 't Veer LJ1, Hooning MJ1, Cornelissen S1, Broeks A1, Rutgers EJ1, Smit VT1, Cornelisse CJ1, van Beek M1, Janssen-Heijnen ML1, Seynaeve C1, **Westenend PJ1**, Jobsen JJ1, Siesling S1, Tollenaar RA1, van Leeuwen FE1, Schmidt MK2.

J Clin Oncol. 2015 Dec 23. pii: JCO623942. [Epub ahead of print]

**PURPOSE:** To determine prospectively overall and age-specific estimates of contralateral breast cancer (CBC) risk for young patients with breast cancer with or without BRCA1/2 mutations.

**PATIENTS AND METHODS:** A cohort of 6,294 patients with invasive breast cancer diagnosed under 50 years of age and treated between 1970 and 2003 in 10 Dutch centers was tested for the most prevalent BRCA1/2 mutations. We report absolute risks and hazard ratios within the cohort from competing risk analyses.

**RESULTS:** After a median follow-up of 12.5 years, 578 CBCs were observed in our study population. CBC risk for BRCA1 and BRCA2 mutation carriers was two to three times higher than for noncarriers (hazard ratios, 3.31 [95% CI, 2.41 to 4.55;  $P < .001$ ] and 2.17 [95% CI, 1.22 to 3.85;  $P = .01$ ], respectively). Ten-year cumulative CBC risks were 21.1% (95% CI, 15.4 to 27.4) for BRCA1, 10.8% (95% CI, 4.7 to 19.6) for BRCA2 mutation carriers and 5.1% (95% CI, 4.5 to 5.7) for noncarriers. Age at diagnosis of the first breast cancer was a significant predictor of CBC risk in BRCA1/2 mutation carriers only; those diagnosed before age 41 years had a 10-year cumulative CBC risk of 23.9% (BRCA1: 25.5%; BRCA2: 17.2%) compared with 12.6% (BRCA1: 15.6%; BRCA2: 7.2%) for those 41 to 49 years of age ( $P = .02$ ); our review of published studies showed ranges of 24% to 31% before age 40 years (BRCA1: 24% to 32%; BRCA2: 17% to 29%) and 8% to 21% after 40 years (BRCA1: 11% to 52%; BRCA2: 7% to 18%), respectively.

**CONCLUSION:** Age at first breast cancer is a strong risk factor for cumulative CBC risk in BRCA1/2 mutation carriers. Considering the available evidence, age-specific risk estimates should be included in counseling.

PMID: 26700119

### **Magnetic Resonance Imaging in Patients with Unilateral Bloody Nipple Discharge; Useful When Conventional Diagnostics are Negative?**

**van Gelder L1, Bisschops RH, Menke-Pluymers MB, Westenend PJ, Plaisier PW.**

World J Surg. 2015 Jan;39(1):184-6. doi: 10.1007/s00268-014-2701-1.

**BACKGROUND:** Unilateral bloody nipple discharge (UBND) is mostly caused by benign conditions such as papilloma or ductal ectasia. However, in 7-33 % of all nipple discharge, it is caused by breast cancer. Conventional diagnostic imaging like mammography (MMG) and ultrasonography (US) is performed to exclude malignancy. Preliminary investigations of breast magnetic resonance imaging (MRI) assume that it has additional value. With an increasing availability of MRI, it is of clinical importance to evaluate this. We evaluated the additional diagnostic value of MRI in patients with UBND in the absence of a palpable mass, with normal conventional imaging.

**METHODS:** All women with UBND in the period November 2007-July 2012 were included. In addition to the standard work-up (patient's history, physical examination, MMG, and US), MRI was performed. Data from these examinations and treatment were collected retrospectively.

**RESULTS:** A total of 111 women (mean age 52 years; range 23-80) were included. In nine (8 %) patients, malignancy was suspected on MRI while conventional imaging was normal. In eight (89 %) of these patients, histology was obtained, two by core biopsy and six by terminal duct excision. Benign conditions were found in six patients (86 %) and a (pre-) malignant lesion in two patients. In both cases, it concerned a ductal carcinoma in situ, which was treated with breast-conserving therapy. Moreover, in two cases of (pre)malignancy, the MRI was interpreted as negative.

**CONCLUSION:** In patients with UBND who show no signs of a malignancy on conventional diagnostic examinations, the added value of a breast MRI is limited, since a malignancy can be demonstrated in <2 %.

PMID: 25123174

### **Multiparametric MRI With Dynamic Contrast Enhancement, Diffusion-Weighted Imaging, and 31-Phosphorus Spectroscopy at 7 T for Characterization of Breast Cancer.**

Schmitz AM1, Veldhuis WB, **Menke-Pluijmers MB**, van der Kemp WJ, van der Velden TA, **Kock MC**, **Westenend PJ**, Klomp DW, Gilhuijs KG.

Invest Radiol. 2015 Nov;50(11):766-71. doi: 10.1097/RLI.000000000000183.

**OBJECTIVES:** To describe and to correlate tumor characteristics on multiparametric 7 tesla (T) breast magnetic resonance imaging (MRI) with prognostic characteristics from postoperative histopathology in patients with breast cancer.

**MATERIALS AND METHODS:** Institutional review board approval and written informed consent of 15 women (46-70 years) with 17 malignant lesions were obtained. In this prospective study (March 2013 to March 2014), women were preoperatively scanned using dynamic contrast-enhanced MRI, diffusion-weighted imaging, and 31-phosphorus spectroscopy (P-MRS).

The value of the protocol was assessed to quantify tumor differentiation and proliferation. Dynamic contrast-enhanced MRI was assessed according to the American College of Radiology Breast Imaging Reporting and Data System-MRI lexicon. Apparent diffusion coefficients (ADCs) were calculated from diffusion-weighted imaging. On P-MRS, at the location of the tumor, the amount of phosphorus components was obtained in a localized spectrum. In this spectrum, the height of phosphodiester (PDE) and phosphomonoester (PME) peaks was assessed to serve as a measure for metabolic activity, stratifying tumors into a PDE > PME, PDE = PME, or PDE < PME group. Tumor grade and mitotic count from resection specimen were compared with the MRI characteristics using explorative analyses.

**RESULTS:** On dynamic contrast-enhanced MRI, the mean tumor size was 24 mm (range, 6-55 mm). An inverse trend was seen between ADC and tumor grade ( $P = 0.083$ ), with mean ADC of  $867 \times 10 \text{ mm}^2/\text{s}$  for grade 1 ( $N = 4$ ),  $751 \times 10 \text{ mm}^2/\text{s}$  for grade 2 ( $N = 6$ ), and  $659 \times 10 \text{ mm}^2/\text{s}$  for grade 3 ( $N = 2$ ) tumors. Between P-MR spectra and mitotic count, a relative increase of PME over PDE showed significant association with increasing mitotic counts ( $P = 0.02$ ); a mean mitotic count of 6 was found in the PDE greater than PME group ( $N = 7$ ), 8 in the PDE = PME group ( $N = 1$ ), and 17 in the PDE < PME group ( $N = 3$ ).

**CONCLUSIONS:** Multiparametric 7 T breast MRI is feasible in clinical setting and shows association between ADC and tumor grade, and between P-MRS and mitotic count.

PMID: 26135017

**SDHB/SDHA immunohistochemistry in pheochromocytomas and paragangliomas: a multicenter interobserver variation analysis using virtual microscopy: a Multi-national Study of the European Network for the Study of Adrenal Tumors (ENS@T).**

Papathomas TG1, Oudijk L2, Persu A3, Gill AJ4, **van Nederveen F5**, Tischler AS6, Tissier F7, Volante M8, Matias-Guiu X9, Smid M10, Favier J11, Rapizzi E12, Libe R13, Currás-Freixes M14, Aydin S15, Huynh T16, Lichtenauer U17, van Berkel A18, Canu L12, Domingues R19, Clifton-Bligh RJ20, Bialas M21, Vikkula M22, Baretton G23, Papotti M8, Nesi G24, Badoual C25, Pacak K16, Eisenhofer G26, Timmers HJ18, Beuschlein F17, Bertherat J27, Mannelli M28, Robledo M29, Gimenez-Roqueplo AP11, Dinjens WN2, Korpershoek E2, de Krijger RR30. *Mod Pathol.* 2015 Jun;28(6):807-21. doi: 10.1038/modpathol.2015.41. Epub 2015 Feb 27.

Despite the established role of SDHB/SDHA immunohistochemistry as a valuable tool to identify patients at risk for familial succinate dehydrogenase-related pheochromocytoma/paraganglioma syndromes, the reproducibility of the assessment methods has not as yet been determined. The aim of this study was to investigate interobserver variability among seven expert endocrine pathologists using a web-based virtual microscopy approach in a large multicenter pheochromocytoma/paraganglioma cohort (n=351): (1) 73 SDH mutated, (2) 105 non-SDH mutated, (3) 128 samples without identified SDH-x mutations, and (4) 45 with incomplete SDH molecular genetic analysis. Substantial agreement among all the reviewers was observed either with a two-tiered classification (SDHB  $\kappa=0.7338$ ; SDHA  $\kappa=0.6707$ ) or a three-tiered classification approach (SDHB  $\kappa=0.6543$ ; SDHA  $\kappa=0.7516$ ). Consensus was achieved in 315 cases (89.74%) for SDHB immunohistochemistry and in 348 cases (99.15%) for SDHA immunohistochemistry. Among the concordant cases, 62 of 69 (~90%) SDHB-/C-/D-/AF2-mutated cases displayed SDHB immunonegativity and SDHA immunopositivity, 3 of 4 (75%) with SDHA mutations showed loss of SDHA/SDHB protein expression, whereas 98 of 105 (93%) non-SDH-x-mutated counterparts demonstrated retention of SDHA/SDHB protein expression. Two SDHD-mutated extra-adrenal paragangliomas were scored as SDHB immunopositive, whereas 9 of 128 (7%) tumors without identified SDH-x mutations, 6 of 37 (~16%) VHL-mutated, as well as 1 of 21 (~5%) NF1-mutated tumors were evaluated as SDHB immunonegative. Although 14 out of those 16 SDHB-immunonegative cases were nonmetastatic, an overall significant correlation between SDHB immunonegativity and malignancy was observed (P=0.00019). We conclude that SDHB/SDHA immunohistochemistry is a reliable tool to identify patients with SDH-x mutations with an additional value in the assessment of genetic variants of unknown significance. If SDH molecular genetic analysis fails to detect a mutation in SDHB-immunonegative tumor, SDHC promoter methylation and/or VHL/NF1 testing with the use of targeted next-generation sequencing is advisable.

PMID: 25720320

**Using a gene expression signature when controversy exists regarding the indication for adjuvant systemic treatment reduces the proportion of patients receiving adjuvant chemotherapy: a nationwide study.**

Kuijjer A1, van Bommel AC2, **Drukker CA3**, van der Heiden-van der Loo M4, Smorenburg CH5, **Westenend PJ6**, Linn SC5, Rutgers EJ7, Elias SG8, van Dalen T1. *Genet Med.* 2015 Nov 19. doi: 10.1038/gim.2015.152. [Epub ahead of print]

PURPOSE: The Dutch national guideline advises use of gene-expression signatures, such as the 70-gene signature (70-GS), in case of ambivalence regarding the benefit of adjuvant

chemotherapy (CT). In this nationwide study, the impact of 70-GS use on the administration of CT in early breast cancer patients with a dubious indication for CT is assessed.

**METHODS:** Patients within a national guideline directed indication area for 70-GS use who were surgically treated between November 2011 and April 2013 were selected from the Netherlands Cancer Registry database. The effect of 70-GS use on the administration of CT was evaluated in guideline- and age-delineated subgroups addressing potential effect of bias by linear mixed-effect modeling and instrumental variable (IV) analyses.

**RESULTS:** A total of 2,043 patients within the indicated area for 70-GS use were included, of whom 298 received a 70-GS. Without use of the 70-GS, 45% of patients received CT. The 70-GS use was associated with a 9.5% decrease in CT administration (95% confidence interval (CI): -15.7 to -3.3%) in linear mixed-effect model analyses and IV analyses showed similar results (-9.9%; 95% CI: -19.3 to -0.4).

**CONCLUSION:** In patients in whom the Dutch national guidelines suggest the use of a gene-expression profile, 70-GS use is associated with a 10% decrease in the administration of adjuvant CT. *Genet Med* advance online publication 19 November 2015 *Genetics in Medicine* (2015);

PMID: 26583684

### Vascular pattern analysis for the prediction of clinical behaviour in pheochromocytomas and paragangliomas.

Oudijk L1, van Nederveen F2, Badoual C3, Tissier F4, Tischler AS5, Smid M6, Gaal J1, Lepoutre-Lussey C7, Gimenez-Roqueplo AP8, Dinjens WN1, Korpershoek E1, de Krijger R9, Favier J7.

*PLoS One*. 2015 Mar 20;10(3):e0121361. doi: 10.1371/journal.pone.0121361. eCollection 2015.

Pheochromocytomas (PCCs) are neuroendocrine tumors arising from chromaffin cells of the adrenal medulla. Related tumors that arise from the paraganglia outside the adrenal medulla are called paragangliomas (PGLs). PCC/PGLs are usually benign, but approximately 17% of these tumors are malignant, as defined by the development of metastases. Currently, there are no generally accepted markers for identifying a primary PCC or PGL as malignant. In 2002, Favier et al. described the use of vascular architecture for the distinction between benign and malignant primary PCC/PGLs. The aim of this study was to validate the use of vascular pattern analysis as a test for malignancy in a large series of primary PCC/PGLs. Six independent observers scored a series of 184 genetically well-characterized PCCs and PGLs for the CD34 immunolabeled vascular pattern and these findings were correlated to the clinical outcome. Tumors were scored as malignant if an irregular vascular pattern was observed, including vascular arcs, parallels and networks, while tumors with a regular pattern of short straight capillaries were scored as benign. Mean sensitivity and specificity of vascular architecture, as a predictor of malignancy was 59.7% and 72.9%, respectively. There was significant agreement between the 6 observers (mean  $\kappa = 0.796$ ). Mean sensitivity of vascular pattern analysis was higher in tumors >5 cm (63.2%) and in genotype cluster 2 tumors (100%). In conclusion, vascular pattern analysis cannot be used in a stand-alone manner as a prognostic tool for the distinction between benign and malignant PCC, but could be used as an indicator of malignancy and might be a useful tool in combination with other morphological characteristics.

PMID: 25794004

## **Progressive valgus deformity of the donor-site ankle after extraperiosteal harvesting the fibular shaft in children. Treatment with osteotomy and synostosis at one session.**

**Van der Veen FJ1**, Strackee SD2, Besselaar PP3.

J Orthop. 2014 Jul 19;12(Suppl 1):S94-S100. doi: 10.1016/j.jor.2014.03.001. eCollection 2015.

After extraperiosteal harvesting of the fibular shaft in children, progressive valgus deformity of the donor-site ankle may pose a serious problem. We present three illustrative case-histories: three children became functionally impaired and required surgery. Pathogenesis, natural history and surgical options are discussed. A supramalleolar osteotomy combined with a distal fibular-tibial synostosis is a good option to correct valgus and eliminate instability in one surgical session. KEYWORDS: Ankle; Donor-site morbidity; Valgus deformity; Vascularized fibular graft

PMID: 26719617

## **Revealing the impact of local access-site complications and upper extremity dysfunction post transradial percutaneous coronary procedures.**

**Zwaan EM1, Koopman AG1, Holtzer CA2, Zijlstra F3, Ritt MJ4, Amoroso G5, Moerman E6, Kofflard MJ1, IJsselmuiden AA7.**

Neth Heart J. 2015 Nov;23(11):514-24. doi: 10.1007/s12471-015-0747-9.

OBJECTIVES: Little is known about local access-site complications and upper extremity dysfunction after transradial percutaneous coronary procedures (TR-PCP). This systematic review study aimed to summarise the current knowledge on the incidences of access-site complications and upper extremity dysfunction after TR-PCP.

METHODS: Two independent, trained investigators searched MEDLINE, EMBASE and CENTRAL for eligible studies published before 1 January 2015. Also, they hand-searched the conference proceedings of the annual scientific sessions of the American College of Cardiology, the American Heart Association, European Society of Cardiology, and the Trans-catheter Cardiovascular Therapeutics. Inclusion criteria were cohort studies and clinical trials discussing the incidence of access-site complications and upper extremity function after transradial percutaneous coronary intervention (TR-PCI) and/or transradial coronary angiography (TR-CAG) as endpoints.

RESULTS: 176 articles described access-site complications. The incidence is up to 9.6%. Fourteen articles described upper extremity dysfunction, with an incidence of up to 1.7%. Upper extremity dysfunction was rarely investigated, hardly ever as primary endpoint, and if investigated not thoroughly enough.

CONCLUSION: Upper extremity dysfunction in TR-PCP has never been properly investigated and is therefore underestimated. Further studies are needed to investigate the magnitude, prevention and best treatment of upper extremity dysfunction. Optimising TR-PCP might be achieved by using slender techniques, detection of upper extremity dysfunction and early referral to a hand rehabilitation centre.

KEYWORDS: Access-site complication; Radial artery; Upper extremity dysfunction

PMID: 26437970

# Psychiatrie

**High frequency of adult attention deficit hyperactivity disorder among fibromyalgia patients in the Netherlands: should a systematic collaboration between rheumatologists and psychiatrists be sought?**

**Derksen MT1, Vreeling MJ, Tchetterikov I.**

Clin Exp Rheumatol. 2015 Jan-Feb;33(1 Suppl 88):S141. Epub 2014 Aug 15.

PMID: 25152225

## **[A man with an abnormal PET-CT scan]. Een man met een afwijkende PET-CT-scan**

**Meulman TJ1, Ho-Han SH, Hendriksz TR.**

Ned Tijdschr Geneeskd. 2015;159(0):A9343.

A 65-year-old patient with rectal carcinoma underwent an 18FDG PET-CT scan. The scan showed nodular foci of 18FDG uptake against the ventral abdominal wall, possibly carcinomatous peritonitis. These abnormalities were caused by a foreign body reaction to a mesh that was placed five months earlier because of an umbilical hernia repair.

PMID: 26507066

## **A randomised controlled trial comparing compression therapy after radiofrequency ablation for primary great saphenous vein incompetence.**

Krasznai A1, Sigterman T2, **Troquay S3**, Houtermans-Auckel J1, Snoeijs M1, Rensma H1, Sikkink C1, Bouwman L1.

Phlebology. 2015 Jan 23. pii: 0268355514568658. [Epub ahead of print]

BACKGROUND: Optimal duration of leg compression after venous ablation remains unclear. This randomised controlled trial evaluates 4 h compared to 72 h of leg compression.

METHODS: Patients were randomised to 4 or 72 h of leg compression after radiofrequency ablation of the great saphenous vein. Primary outcome was change in leg volume after 14 days. Secondary outcomes were postoperative pain, complications and time to full recovery.

RESULTS: Patients wearing compression stockings for 4 h after treatment had a 64 mL (95%CI: -23 to +193) reduction in leg volume, compared to an increase of 21 mL (95%CI: 8.33-34.5) in patients wearing compression stockings for 72 h (P=0.12). Patients wearing compression stockings for 4 h experienced fewer complications (16% vs. 33%, P=0.05).

Postoperative pain and time to full recovery did not differ significantly.

CONCLUSION: Wearing compression stockings for 4 h is non-inferior in preventing leg oedema as wearing compression stockings for 72 h. © The Author(s) 2015 Reprints and permissions: [sagepub.co.uk/journalsPermissions.nav](http://sagepub.co.uk/journalsPermissions.nav).

KEYWORDS: Compressive therapy; endovenous therapy; radiofrequency ablation

PMID: 25616874

## **Coaching Reduced the Radiation Dose of Pain Physicians by Half during Interventional Procedures.**

**Slegers AS1, Gültuna I, Aukes JA, van Gorp EJ, Blommers FM, Niehof SP, Bosman J.**

Pain Pract. 2015 Jun;15(5):400-6. doi: 10.1111/papr.12251. Epub 2014 Oct 29.

The increased use of C-arm fluoroscopy in interventional pain management has led to higher radiation exposure for pain physicians. This study investigated whether or not real-time radiation dose feedback with coaching can reduce the scatter dose received by pain physicians. Firstly, phantom measurements were made to create a scatter dose profile, which visualizes the

average scatter radiation for different C-arm positions at 3 levels of height. Secondly, in the clinical part, the radiation dose received by pain physicians during pain treatment procedures was measured real-time to evaluate (1) the effect of real-time dose feedback on the received scatter dose, and (2) the effect of knowledge of the scatter dose profile and active coaching, on the scatter dose received by the pain physician. The clinical study included 330 interventional pain procedures. The results showed that real-time feedback of the received dose did not lead to a reduction in scatter radiation. However, visualization of the scatter dose in a scatter dose profile and active coaching on optimal positions did reduce the scatter radiation received by pain physicians during interventional pain procedures by 46.4% ( $P = 0.05$ ). Knowledge of and real-time coaching with the scatter dose profile reduced the dose of pain physicians by half, caused by their increased awareness for scatter radiation and their insight into strategic positioning.

PMID: 25354342

### [Diagnostic imaging in dementia: use of imaging modalities in Dutch memory clinics].

**Gardeniers M1**, Wattjes MP2, **Meulen EF3**, Barkhof F2, **Bakker J4**.

Tijdschr Gerontol Geriatr. 2015 Nov 2. [Epub ahead of print]

**PURPOSE:** To evaluate the use of MRI and CT in the diagnostic work-up of dementia in Dutch memory clinics, and to analyse the rationale for choosing each modality.

**MATERIALS AND METHODS:** A digital survey was sent by e-mail to all medical specialists ( $n=235$ ) working at a memory clinic in the Netherlands.

**RESULTS:** The survey was completed by 64% (151). 85% of the respondents were geriatricians, 13% neurologists and 2% other, working at a total of 69 clinics. 40% variably orders CT or MRI, 37% orders MRI, 19% CT, and 4% CT plus MRI. Primary factors influencing this choice are: MRI contraindications, physical limitations, age, vascular or oncological medical history, and waiting time. With CT, 87% indicates information is lacking: vascular disease/white matter lesions, (hippocampal) atrophy, and specific pathologies (metastases, amyloid angiopathy). Furthermore, respondents prefer MRI because they can assess the images more easily themselves. Only 50% of respondents indicate that CT protocol dictates coronal reconstructions. Additionally, these reconstructions are not provided consistently. Rating-scales are used to describe images in 5%. In 75% assessment is not uniform.

**CONCLUSION:** MRI is preferred over CT in diagnostic imaging of dementia, in accordance with existing guidelines. However, these guidelines are mostly out-dated and modern multislice CT potential is relatively unknown among geriatricians. In memory clinics, multislice CT could offer a well suitable imaging alternative, but only if multiplanar reconstructions are performed consistently. Furthermore, radiology reports need to be improved by using more standardized assessment.

PMID: 26525706

### Is aortoiliac calcification linked to colorectal anastomotic leakage?

#### A case-control study.

Boersema GS1, Vakalopoulos KA2, **Kock MC3**, van Ooijen PM4, Havenga K5, Kleinrensink GJ6, Jeekel J6, Lange JF2.

Int J Surg. 2015 Dec 14;25:123-127. doi: 10.1016/j.ijsu.2015.12.008. [Epub ahead of print]

**BACKGROUND:** Anastomotic leakage in bowel surgery remains a devastating complication. Various risk factors have been uncovered, however, high anastomotic leakage rates are still being reported. This study describes the use of calcification markers of the central abdominal arteries as a prognostic factor for colorectal anastomotic leakage.

**METHODS:** This case-control study includes clinical data from three different hospitals. Calcium volume and calcium score of the aortoiliac tract were determined by CT-scan analysis. Cases were all patients with anastomotic leakage after a left-sided anastomosis (n=30). Three controls were randomly matched for each case. Only patients with a contrast-enhanced pre-operative CT-scan were included.

**RESULTS:** The measurements of the calcium score and calcium volume of the different trajectories showed that there was one significant difference with regard to the right external iliac artery. Multiple regression analysis showed a significant different negative odds ratio of the presence of calcium in the right external iliac artery.

**CONCLUSION:** This study demonstrates that calcium volume and calcium score of the aortoiliac trajectory does not correlate with the risk of colorectal anastomotic leakage after a left-sided anastomosis. Copyright © 2015. Published by Elsevier Ltd.

**KEYWORDS:** Anastomotic leakage; Calcium score; Calcium volume; Colorectal surgery; Prognostic factor

PMID: 26700199

### **Ischemic cardiomyopathy and cerebral infarction in a young patient associated with khat chewing.**

**Meulman TJ1, Bakker J1, van den Bos EJ2.**

Case Rep Radiol. 2015;2015:893176. doi: 10.1155/2015/893176. Epub 2015 Feb 26.

Khat is a stimulating agent used by many people in the Horn of Africa and the Arabian peninsula. Khat chewing is a known cardiovascular risk factor and is thought to cause vasoconstriction, systemic hypertension, and thrombogenicity. A 33-year-old Somalian man initially presented with loss of neurological function of the left arm, hazy vision, and headache. He smokes tobacco and chews two bundles of khat a week for more than 10 years. His ECG on admission showed a Q wave in V1 and V2 and 2mm ST-elevations in V1, V2, and V3 and a terminal negative T wave in I, aVL, V2, V3, and V4, consistent with a recent, evolving anterior infarction. A noncontrast enhanced CT of the brain showed ischemia in the right middle cerebral artery vascular territory. An MRI showed recent ischemia in the vascular territory of the posterior division of the right middle cerebral artery. Coronary angiography showed a 70% stenosis with haziness of the proximal left anterior descending artery. Diagnostic tests and imaging are consistent with recent myocardial infarction in the LAD vascular territory because of coronary spasm and cerebral infarction in the middle cerebral artery vascular territory probably related to khat chewing.

PMID: 25815235

### **Knee instability in patients with traumatic knee disorders: a cohort study in primary care.**

Luijsterburg PA1, Wagemakers HP2, Kastelein M2, Verhaar JA3, **Koster IM4**, Oei EH5, Koes BW2, Bierma-Zeinstra SM6.

Fam Pract. 2015 Aug;32(4):367-73. doi: 10.1093/fampra/cmz023. Epub 2015 Apr 22.

**BACKGROUND:** There is a lack of knowledge about the course of knee instability in patients with traumatic knee disorders.

**OBJECTIVE:** The aim of the study was to determine the course of traumatic knee instability during 1-year follow-up and to observe the treatment of knee instability by GPs.

**METHODS:** Patients (n = 134) aged 18-65 years with traumatic knee disorders who consulted their GP within 5 weeks after trauma were enrolled in a prospective cohort study. Data were collected at baseline and at 3, 6 and 12 months follow-up. Magnetic resonance imaging (MRI) and physical examination of the knee were performed at baseline and at 1-year follow-up.

**RESULTS:** At baseline, 28% of the 134 patients had no knee instability, 17% reported knee instability (according Lysholm score), 31% tested positive on knee instability (according Lachman test) and 24% both self-reported and tested positive on instability of the knee. At baseline and at 1-year follow-up, no clear differences between MRI findings, treatment and course of the defined groups of knee instability were found. At 1-year follow-up, patients with both self-reported and tested positive seemed to have worse outcomes.

**CONCLUSION:** During 1-year follow-up, it was unclear if there were differences regarding course, treatment and MRI findings of the knee between no instability and the three defined knee instability groups. Statistical power was lacking in the comparisons made and therefore studies with more patients are needed. © The Author 2015. Published by Oxford University Press. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

**KEYWORDS:** Cohort study; MRI; general practice; musculoskeletal disorder; primary care; traumatic knee disorders.

PMID: 25902913

### **Magnetic Resonance Imaging in Patients with Unilateral Bloody Nipple Discharge; Useful When Conventional Diagnostics are Negative?**

**van Gelder L1, Bisschops RH, Menke-Pluymers MB, Westenend PJ, Plaisier PW.**

World J Surg. 2015 Jan;39(1):184-6. doi: 10.1007/s00268-014-2701-1.

**BACKGROUND:** Unilateral bloody nipple discharge (UBND) is mostly caused by benign conditions such as papilloma or ductal ectasia. However, in 7-33 % of all nipple discharge, it is caused by breast cancer. Conventional diagnostic imaging like mammography (MMG) and ultrasonography (US) is performed to exclude malignancy. Preliminary investigations of breast magnetic resonance imaging (MRI) assume that it has additional value. With an increasing availability of MRI, it is of clinical importance to evaluate this. We evaluated the additional diagnostic value of MRI in patients with UBND in the absence of a palpable mass, with normal conventional imaging.

**METHODS:** All women with UBND in the period November 2007-July 2012 were included. In addition to the standard work-up (patient's history, physical examination, MMG, and US), MRI was performed. Data from these examinations and treatment were collected retrospectively.

**RESULTS:** A total of 111 women (mean age 52 years; range 23-80) were included. In nine (8 %) patients, malignancy was suspected on MRI while conventional imaging was normal.

In eight (89 %) of these patients, histology was obtained, two by core biopsy and six by terminal duct excision. Benign conditions were found in six patients (86 %) and a (pre-) malignant lesion in two patients. In both cases, it concerned a ductal carcinoma in situ, which was treated with breast-conserving therapy. Moreover, in two cases of (pre)malignancy, the MRI was interpreted as negative.

**CONCLUSION:** In patients with UBND who show no signs of a malignancy on conventional

diagnostic examinations, the added value of a breast MRI is limited, since a malignancy can be demonstrated in <2 %.

PMID: 25123174

### **Multiparametric MRI With Dynamic Contrast Enhancement, Diffusion-Weighted Imaging, and 31-Phosphorus Spectroscopy at 7 T for Characterization of Breast Cancer.**

Schmitz AM1, Veldhuis WB, **Menke-Pluijmers MB**, van der Kemp WJ, van der Velden TA, **Kock MC, Westenend PJ**, Klomp DW, Gilhuijs KG.

Invest Radiol. 2015 Nov;50(11):766-71. doi: 10.1097/RLI.000000000000183.

**OBJECTIVES:** To describe and to correlate tumor characteristics on multiparametric 7 tesla (T) breast magnetic resonance imaging (MRI) with prognostic characteristics from postoperative histopathology in patients with breast cancer.

**MATERIALS AND METHODS:** Institutional review board approval and written informed consent of 15 women (46-70 years) with 17 malignant lesions were obtained. In this prospective study (March 2013 to March 2014), women were preoperatively scanned using dynamic contrast-enhanced MRI, diffusion-weighted imaging, and 31-phosphorus spectroscopy (P-MRS). The value of the protocol was assessed to quantify tumor differentiation and proliferation. Dynamic contrast-enhanced MRI was assessed according to the American College of Radiology Breast Imaging Reporting and Data System-MRI lexicon. Apparent diffusion coefficients (ADCs) were calculated from diffusion-weighted imaging. On P-MRS, at the location of the tumor, the amount of phosphorus components was obtained in a localized spectrum. In this spectrum, the height of phosphodiester (PDE) and phosphomonoester (PME) peaks was assessed to serve as a measure for metabolic activity, stratifying tumors into a PDE > PME, PDE = PME, or PDE < PME group. Tumor grade and mitotic count from resection specimen were compared with the MRI characteristics using explorative analyses.

**RESULTS:** On dynamic contrast-enhanced MRI, the mean tumor size was 24 mm (range, 6-55 mm). An inverse trend was seen between ADC and tumor grade ( $P = 0.083$ ), with mean ADC of  $867 \times 10 \text{ mm}^2/\text{s}$  for grade 1 ( $N = 4$ ),  $751 \times 10 \text{ mm}^2/\text{s}$  for grade 2 ( $N = 6$ ), and  $659 \times 10 \text{ mm}^2/\text{s}$  for grade 3 ( $N = 2$ ) tumors. Between P-MR spectra and mitotic count, a relative increase of PME over PDE showed significant association with increasing mitotic counts ( $P = 0.02$ ); a mean mitotic count of 6 was found in the PDE greater than PME group ( $N = 7$ ), 8 in the PDE = PME group ( $N = 1$ ), and 17 in the PDE < PME group ( $N = 3$ ).

**CONCLUSIONS:** Multiparametric 7 T breast MRI is feasible in clinical setting and shows association between ADC and tumor grade, and between P-MRS and mitotic count.

PMID: 26135017

### **Magnetic resonance imaging abnormalities after lateral ankle trauma in injured and contralateral ankles.**

**van Putte-Katier N1**, van Ochten JM2, van Middelkoop M2, Bierma-Zeinstra SM2, Oei EH3. Eur J Radiol. 2015 Dec;84(12):2586-92. doi: 10.1016/j.ejrad.2015.09.028. Epub 2015 Oct 9.

**PURPOSE:** To compare the prevalence of abnormal MRI findings associated with lateral ankle trauma in injured and contralateral ankles to identify lesions that may be pre-existent.

**MATERIAL AND METHODS:** The study was approved by the institutional review board and informed consent was obtained from all subjects. 195 patients (mean age  $37.5 \pm 14.7$  years;

43% male) who visited their general practitioner 6-12 months earlier with an ankle sprain were selected. All patients completed a standardized questionnaire and underwent MRI (1.5T) of both ankles. Structural MRI abnormalities in the injured and contralateral ankle were compared using the McNemar test (for paired samples).

**RESULTS:** Bone marrow edema was frequently seen in the injured and contralateral ankle at the talocrural joint (25.1% versus 14.8%) and subtalar joint (24.6% versus 8.7%), but significantly more frequently in the injured ankle. Anterior talofibular ligament (ATFL) and calcaneofibular ligament (CFL) lesions were frequently found in both ankles, in 55.9% and 37.4% of injured ankles respectively and in 17.9% and 5.6% of contralateral ankles respectively. Fractures, anterior and posterior tibiofibular ligament lesions, deltoid ligament lesions and signs of talonavicular osteoarthritis were almost exclusively found in injured ankles. Peroneal ligament lesions were not frequently found in both ankles.

**CONCLUSIONS:** The prevalence of structural MRI abnormalities in patients presenting with a previous ankle sprain in primary care is very high. However, especially bone marrow edema and lateral ligament lesions can also be found in a substantial percentage of contralateral ankles and may be either pre-existent or due to increased stress on the contralateral ankle after an ankle injury. Correlation with clinical findings is essential.

**KEYWORDS:** Abnormalities; Ankle; General practice; Imaging; Sprain

PMID: 26456306

### **MR Imaging as an Additional Screening Modality for the Detection of Breast Cancer in Women Aged 50-75 Years with Extremely Dense Breasts: The DENSE Trial Study Design.**

Emaus MJ<sup>1</sup>, Bakker MF<sup>1</sup>, Peeters PH<sup>1</sup>, Loo CE<sup>1</sup>, Mann RM<sup>1</sup>, de Jong MD<sup>1</sup>, **Bisschops RH<sup>1</sup>**, Veltman J<sup>1</sup>, Duvivier KM<sup>1</sup>, Lobbes MB<sup>1</sup>, Pijnappel RM<sup>1</sup>, Karssemeijer N<sup>1</sup>, de Koning HJ<sup>1</sup>, van den Bosch MA<sup>1</sup>, Monnikhof EM<sup>1</sup>, Mali WP<sup>1</sup>, Veldhuis WB<sup>1</sup>, van Gils CH<sup>1</sup>.  
Radiology. 2015 Nov;277(2):527-37. doi: 10.1148/radiol.2015141827. Epub 2015 Jun 23.

Women with extremely dense breasts have an increased risk of breast cancer and lower mammographic tumor detectability. Nevertheless, in most countries, these women are currently screened with mammography only. Magnetic resonance (MR) imaging has the potential to improve breast cancer detection at an early stage because of its higher sensitivity. However, MR imaging is more expensive and is expected to be accompanied by an increase in the number of false-positive results and, possibly, an increase in overdiagnosis. To study the additional value of MR imaging, a randomized controlled trial (RCT) design is needed in which one group undergoes mammography and the other group undergoes mammography and MR imaging. With this design, it is possible to determine the proportion of interval cancers within each study arm. For this to be an effective screening strategy, the additional cancers detected at MR imaging screening must be accompanied by a subsequent reduction in interval cancers. The Dense Tissue and Early Breast Neoplasm Screening, or DENSE, trial is a multicenter RCT performed in the Dutch biennial population-based screening program (subject age range, 50-75 years). The study was approved by the Dutch Minister of Health, Welfare and Sport. In this study, mammographic density is measured by using a fully automated volumetric method. Participants with extremely dense breasts (American College of Radiology breast density category 4) and a negative result at mammography (Breast Imaging Recording and Data System category 1 or 2) are randomly assigned to undergo additional MR imaging (n = 7237) or to be treated according to current practice (n = 28 948). Participants provide written informed consent before the MR imaging examination, which consists of dynamic breast MR imaging with

gadolinium-based contrast medium and is intended to be performed for three consecutive screening rounds. The primary outcome is the difference in the proportions of interval cancers between the study arms. Secondary outcomes are the number of MR imaging screening-detected cancers, proportions of false-positive results, diagnostic yield of MR imaging, tumor characteristics, quality of life, and cost effectiveness. (©) RSNA, 2015.

PMID: 26110667

### Sigmoid Cancer versus Chronic Diverticular Disease: Differentiating Features at CT Colonography.

Lips LM1, Cremers PT, Pickhardt PJ, **Cremers SE**, Janssen-Heijnen ML, de Witte MT, Simons PC. (ASz bijdrage??)

Radiology. 2015 Apr;275(1):127-35. doi: 10.1148/radiol.14132829. Epub 2014 Nov 26.

**PURPOSE:** To retrospectively identify morphologic findings at computed tomographic (CT) colonography that are the most reliable in the differentiation of masslike chronic diverticular disease from sigmoid carcinoma in a large patient cohort.

**MATERIALS AND METHODS:** This study was approved by the institutional review boards. The need for signed consent was waived for this retrospective study. The cohort consisted of 212 patients (mean age, 68 years; 113 women, 99 men) with focal masslike findings in the sigmoid colon at CT colonography, representing chronic diverticular disease (n = 97) or sigmoid carcinoma (n = 115). CT colonography studies were scored according to presence or absence of potential discriminators by a panel of four readers in consensus. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated, and multivariate analysis was performed.

**RESULTS:** Absence of diverticula in the affected segment showed high NPV and PPV (0.95 and 0.93, respectively). Also, shoulder phenomenon showed a high NPV (0.92) and PPV (0.75). Segment length of 10 cm or less (NPV, 0.85; PPV, 0.61) and destroyed mucosal folds (NPV, 1.00; PPV, 0.62) had a high NPV but a low PPV. Although segments affected by carcinoma often showed straightened and eccentric growth patterns, no thick fascia sign, and more and larger local-regional lymph nodes (all  $P < .05$ ), NPV was insufficient for discrimination (NPV  $\leq$  0.66). Combination of absence of diverticula and presence of shouldering showed a high diagnostic certainty (93%).

**CONCLUSION:** Carcinoma is best differentiated from masslike diverticular disease by the absence of diverticula in the affected segment and the presence of shoulder phenomenon.

PMID: 25426771

### The don't know option in progress testing

Ravesloot CJ1, Van der Schaaf MF, Muijtjens AM, Haaring C, Kruitwagen CL, Beek FJ, **Bakker J**, Van Schaik JP, Cate TJ.

Adv Health Sci Educ Theory Pract. 2015 Dec;20(5):1325-38. doi: 10.1007/s10459-015-9604-2. Epub 2015 Apr 26.

Formula scoring (FS) is the use of a don't know option (DKO) with subtraction of points for wrong answers. Its effect on construct validity and reliability of progress test scores, is subject of discussion. Choosing a DKO may not only be affected by knowledge level, but also by risk taking tendency, and may thus introduce construct-irrelevant variance into the knowledge measurement. On the other hand, FS may result in more reliable test scores. To evaluate the

impact of FS on construct validity and reliability of progress test scores, a progress test for radiology residents was divided into two tests of 100 parallel items (A and B). Each test had a FS and a number-right (NR) version, A-FS, B-FS, A-NR, and B-NR. Participants (337) were randomly divided into two groups. One group took test A-FS followed by B-NR, and the second group test B-FS followed by A-NR. Evidence for impaired construct validity was sought in a hierarchical regression analysis by investigating how much of the participants' FS-score variance was explained by the DKO-score, compared to the contribution of the knowledge level (NR-score), while controlling for Group, Gender, and Training length. Cronbach's alpha was used to estimate NR and FS-score reliability per year group. NR score was found to explain 27 % of the variance of FS [ $F(1,332) = 219.2, p < 0.0005$ ], DKO-score, and the interaction of DKO and Gender were found to explain 8 % [ $F(2,330) = 41.5, p < 0.0005$ ], and the interaction of DKO and NR 1.6 % [ $F(1,329) = 16.6, p < 0.0005$ ], supporting our hypothesis that FS introduces construct-irrelevant variance into the knowledge measurement. However, NR-scores showed considerably lower reliabilities than FS-scores (mean year-test group Cronbach's alphas were 0.62 and 0.74, respectively). Decisions about FS with progress tests should be a careful trade-off between systematic and random measurement error. Keywords: Construct-irrelevant variance– Construct validity– Don't know option– Formula scoring– Progress testing– Reliability– Risk-taking tendency

PMID: 25912621

# Reumatologie

## **Do we need to lower the cut point of the 2010 ACR/EULAR classification criteria for diagnosing rheumatoid arthritis?**

van der Ven M1, Alves C2, Luime JJ2, Gerards AH3, Barendregt PJ4, van Zeben D5, **van Schaeybroeck B6**, de Sonnaville PB7, Grillet BA8, Hazes JM2.  
Rheumatology (Oxford). 2015 Nov 4. pii: kev383. [Epub ahead of print]

**OBJECTIVE:** In this study we aimed to evaluate the effect of lowering the cut point of the 2010 criteria to identify more patients with RA among early inflammatory arthritis patients. **METHODS:** We included early arthritis patients from the Rotterdam Early Arthritis Cohort with at least one joint with clinical synovitis and symptoms for <1 year, with no other explanation for their symptoms. The demographic and clinical characteristics of each patient were recorded at baseline. Patients were classified as case or non-case at the 1-year follow-up by the definition used in the development of the 2010 criteria (MTX initiation). To assess the diagnostic performance of the 2010 criteria, the sensitivity and specificity at each cut point were determined. **RESULTS:** We included 557 patients in our analysis. At the 1-year follow-up, 253 patients (45%) were classified as case (MTX use). In the group of patients who scored 0-5 points (n = 328), 98 patients (30%) were classified as case (MTX use). The sensitivity and specificity of the 2010 criteria using the cut point of 6 were 61% and 76%, respectively. With the cut point of 5, the sensitivity would increase to 76% and the specificity would decrease to 68%. **CONCLUSION:** By lowering the cut point of the 2010 criteria from 6 to 5 points, we were able to identify 15% more RA patients at the cost of 8% more false-positive patients. © The Author 2015. Published by Oxford University Press on behalf of the British Society for Rheumatology. All rights reserved. For Permissions, please email: journals.permissions@oup.com.

**KEYWORDS:** classification criteria; diagnostic criteria; rheumatoid arthritis

PMID: 26538422

## **High frequency of adult attention deficit hyperactivity disorder among fibromyalgia patients in the Netherlands: should a systematic collaboration between rheumatologists and psychiatrists be sought?**

**Derksen MT1, Vreeling MJ, Tchvetverikov I.**

Clin Exp Rheumatol. 2015 Jan-Feb;33(1 Suppl 88):S141. Epub 2014 Aug 15.

PMID: 25152225

### **Methotrexate polyglutamates in erythrocytes are associated with lower disease activity in patients with rheumatoid arthritis.**

de Rotte MC1, den Boer E1, de Jong PH2, Pluijm SM3, Calasan MB4, Weel AE5, Huisman AM6, Gerards AH7, **van Schaeybroeck B8**, Wulffraat NM4, Lindemans J1, Hazes JM2, de Jonge R1.

Ann Rheum Dis. 2015 Feb;74(2):408-14. doi: 10.1136/annrheumdis-2013-203725.

Epub 2013 Dec 2.

**OBJECTIVE:** To investigate if erythrocyte-methotrexate-polyglutamate (MTX-PG) concentrations in patients with rheumatoid arthritis (RA) are associated with disease activity or adverse events. **METHODS:** We used a longitudinal study design with two cohorts. The derivation cohort included 102 and the validation cohort included 285 patients with RA on MTX. We measured erythrocyte-MTX-PG with 1-5 glutamate residues at 3 months, 6 months and 9 months after MTX start with a liquid chromatography (LC)-mass spectrometry (MS)/MS assay. Outcomes were disease activity score in 28 joints (DAS28) and adverse events. Longitudinal associations of MTX-PG concentrations after 3 months, 6 months and 9 months with DAS28 were tested with a linear mixed model adjusted for age, gender, baseline DAS28, MTX dose and comedication. **RESULTS:** In the derivation cohort, mean DAS28 decreased from 4.26 (SE=0.14) at baseline to 2.72 (SE=0.13) after 9 months. Thirty per cent of patients in the derivation cohort experienced more than three adverse events after 3 months, which decreased to 18% after 9 months. In the validation cohort, DAS28 and adverse events were comparable with the derivation cohort. In the derivation cohort, MTX-PG1 ( $\beta=-0.005$ ), MTX-PG2 ( $\beta=-0.022$ ), MTX-PG3 ( $\beta=-0.007$ ) and total MTX-PG ( $\beta=-0.004$ ) were associated ( $p<0.05$ ) with lower DAS28 over 9 months. In the validation cohort, MTX-PG2 ( $\beta=-0.015$ ), MTX-PG3 ( $\beta=-0.010$ ), MTX-PG4 ( $\beta=-0.008$ ) and total MTX-PG ( $\beta=-0.003$ ) were associated with lower DAS28 over 9 months. None of the MTX-PGs was associated with adverse events. **CONCLUSIONS:** In this first longitudinal study, we showed that an increase in erythrocyte-MTX-PG concentration was associated with a decreased DAS28 over 9 months in two cohorts, and is therefore a potential tool for therapeutic drug monitoring of MTX in RA. Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to <http://group.bmj.com/group/rights-licensing/permissions>. **KEYWORDS:** DMARDs (synthetic); Pharmacokinetics; Rheumatoid Arthritis

PMID: 24297383

### **Prevalence of Psoriatic Arthritis in Primary Care Patients with Psoriasis.**

Karreman MC1, Weel AE1,2, van der Ven M1, Vis M1, **Tchetverikov I3**, Nijsten TE4, Wakkee M4, Hazes JM1, Luime JJ1.

Arthritis Rheumatol. 2015 Dec 4. doi: 10.1002/art.39530. [Epub ahead of print]

**OBJECTIVE:** To estimate the prevalence of PsA in primary care patients diagnosed with psoriasis. The second objective was to estimate the prevalence of MSC in primary care psoriasis patients.

**METHODS:** We conducted a cross-sectional study in adult primary care patients with psoriasis. Responding patients reporting pain in joints, entheses or lower back were checked on eligibility by a telephone interview and invited for clinical evaluation. During clinical evaluation skin, nails, joints and entheses were assessed. Additionally, ultrasonography of the enthesis was performed by an independent trained examiner if a patient had at least one tender enthesis (LEI/MASES). A patient had PsA if fulfilling the CASPAR criteria.

RESULTS: 2564 psoriasis patients from 97 GPs were invited. Of the 1673 responders (65.2%), 841 (50.3%) were willing to participate. 823 (32.1%) patients reported suffering from MSC of which eventually 524 were eligible and clinically evaluated. Sixty-four cases of established PsA were identified and another 17 cases of PsA were newly diagnosed, leading to a prevalence of 3.2% (95%CI 2.5%-3.9%) among primary care psoriasis patients. This would increase towards 4.6% (95% CI 3.8%-5.4%) if the PsA cases based on enthesitis are also taken into account.

CONCLUSION: Among psoriasis patients in primary care the prevalence of PsA is conservatively estimated to be 3.2% increasing to 4.6% if enthesitis is taken into account. The prevalence of MSC in psoriasis patients is comparable to the prevalence in general population. This article is protected by copyright. All rights reserved.

PMID: 26636745

## **Deel III**

# **Overige wetenschappelijke output 2015**

Per vakgroep

# Anesthesiologie

## Overige Publicaties

The role of fibrinogen in massive postpartum haemorrhage, a case report  
Minde M.R.C. van, **Koopman-van Gemert A.W.M.M.**, Rombout-deWeerd S.  
Case Reports in Women's Health 6 (2015) 4–5.

Autotransfusie bij heup- en knieervanging zinvol?  
Bodegom-Vos L. van, Voorn V.M., So-Osman C., Vliet Vlieland T.P., Dahan A.,  
**Koopman-van Gemert AW**, Vehmeijer S.B., Nelissen R.G., Marang-van de Mheen P.J.  
Besproken door Pualine Heus en Karin P.M. van Galen.  
Ned Tijdschr Geneesk 2015; 159 (34): 1452.

Refresher Course: PDPH, an update RAPM, vol 40  
**Schyns-van den Berg AM.**,  
sept/oct 2015, supplement , ESRAS 0543, pp e45-e47,

Protocol Massaal Bloedverlies.  
**Koopman-van Gemert AWMM.**  
Nederlands Tijdschrift voor Anesthesiologie 2015; 27: 137-145

## Voordrachten op geaccrediteerde wetenschappelijke congressen

Bloedtransfusie en bloedbesparende technieken  
**Koopman-van Gemert A.W.M.M.**  
6 januari 2015. EMC te Rotterdam

Workshop locoregionale anesthesie bij Myanmar Medical Association.  
**Falieres X.**  
National congress anesthesiology Yangon, Myanmar, Birma, 5 t/m 7 feb 2015

Workshop Patiëntveiligheid, wat houdt dit in voor de opleiding?  
**Koopman-van Gemert A.W.M.M.** en Rooyen den C.  
11 maart 2015 te IJssellandziekenhuis Rotterdam

Spoed Interventie Team of Reanimatie Team?  
**So K.L.**  
12e National Reanimatie Congres 11 maart 2015 Nieuwegein

Gastcollege over taken en rollen medisch manager Kwaliteit.  
**So K.L.**  
NFU Masteropleiding Kwaliteit en Veiligheid in de Patiëntenzorg 12 maart 2015 Amsterdam

Twee Workshops CRM te EMT Center NVSHA Emergency Medicine Teaching.  
**Koopman-van Gemert A.W.M.M.**  
Second Congress Emergency Cardiology 26 en 27 maart 2015 te ASz Dordrecht

Pijn bestrijding na een Sectio Caesarea, Refresher Course Obstetrische Anesthesie. Normale en Pathologische Zwangerschap.

**Schyns-van den Berg A.M.J.V.**

Faculty Club Leuven, België, 2 april 2015

Vroege herkenning en behandeling van vitaal bedreigde patiënt: 3 casus.

**So K.L.**

Verander het veiligheidsdenken in ziekenhuizen, 16 april 2015 Ede

Neuraxisblokkade en Antistolling.

**Koopman-van Gemert A.W.M.M..**

Refereeravond Anesthesiologie "Neuroblokkades/Antistolling" 12 mei 2015 te Maastricht School of Management (naast AZM) Maastricht

Human factors and their impact on patients and staff outcomes.

**So K.L..**

Preconference course: 11th Int Congress on Rapid Response Teams and Medical Emergency Teams. 18-19 mei 2015. Amsterdam

Reviewer abstracts.

**Barneveld van J.C.**

BMJ International Forum on Quality & Safety in health Care. April 2015 London, Engeland

Continuous Monitoring on the surgical ward.

**So K.L.**

11th Int Congress on Rapid Response Teams and Medical Emergency Teams. 18-19 mei 2015 Amsterdam

Nieuwe orale anticoagulantia (NOACs) en de actuele status van de Richtlijn Neuraxisblokkade en Antistolling"

**Koopman-van Gemert A.W.M.M.**

NVA-cursus 18 en 19 mei 2015. Golden Tulip Doorwerth

Long term outcome of subcutaneous stimulation as an additional therapy to Spinal Cord Stimulation for the treatment of low back and leg pain in patients with Failed Back Surgery Syndrome.

**Hamm-Faber T.E. MA-ANP, Aukes J.A. MD, van Gorp van E.J.J.A.A. MD, Gültuna I. MD.**

World congress INS (International Neuromodulation Society) Montreal, Canada. 10 June 2015

Subcutaneous stimulation as ADD-ON therapy to SCS is effective in treating low back pain in patients with Failed Back Surgery Syndrome: a multicenter randomized controlled trial.

**Gorp van E.J.J.A.A.,** K.Burger, R.Schapendonk, J.Kallewaard, G.Spincemaile, Hamm-Faber T.E.I. vonhogen Jan.CM. Hendriks, Kris.Vissers

10 Juni 2015 World congress INS (International Neuromodulation Society) Montreal, Canada.

Perifere behandelingen.

**Gültuna I.**

Minisymposium "Ons PBC: toonaangevend in de wereld van pijnbehandelingen.

17 juni 2015 te Maria Johanna Hoeve te Noordeloos.

Intradiscale behandelingen.

**Aukes J.A.**

Minisymposium "Ons PBC: toonaangevend in de wereld van pijnbehandelingen.

17 juni 2015 te Maria Johanna Hoeve te Noordeloos.

Wetenschappelijke studies.

**Hamm-Faber T.E. (VS BPC).**

Minisymposium "Ons PBC: toonaangevend in de wereld van pijnbehandelingen.

17 juni 2015 te Maria Johanna Hoeve te Noordeloos.

Promotie-onderzoek.

**Gorp van E.J.J.A.A.** Minisymposium "Ons PBC: toonaangevend in de wereld van

pijnbehandelingen. 17 juni 2015 te Maria Johanna Hoeve te Noordeloos.

Oncologische pijn.

**Kersten S. (VS PBC).**

Minisymposium "Ons PBC: toonaangevend in de wereld van pijnbehandelingen.

17 juni 2015 te Maria Johanna Hoeve te Noordeloos.

Training ambassadeurs in patiëntveiligheid.

Ham J.J., **Koopman-van Gemert A.W.M.M.**, Gans R.O.P. Rooyen den C.. Driel van P.

Ernst Sillem Hoeve te Den Dolder 18 en 19 juni 2015

Cutaneous mitochondrial PO<sub>2</sub> is an early indicator of the physiological limit of hemodilution in the pig.

**Römers L.H.L.**, aios anesthesiologie.

Wetenschapsdag ASz, 18 juni 2015

Auditorium ASz Dordrecht

Het effect van vroege identificatie van en respons op de vitaal bedreigde patiënt door het gebruik van continue monitoring op mortaliteit: is er een weekend effect?

**So K.L.**

Wetenschapsdag ASz, 18 juni 2015.

Auditorium ASz Dordrecht

Reviewer abstracts.

**Koopman-van Gemert A.W.M.M..**

ISBT 25th regional Congress 2015 London, Engeland

PDPH: an update and discussion.

**Schyns-van den Berg A.M.J.V**

Refresher Course ESRA, 2/7 september 2015 Ljubljana, Slovenie

Alternative strategies for labour pain relief.

**Schyns-van den Berg A.M.J.V.**

ESRA, 2/7 september 2015 Ljubljana, Slovenie

Peripheral electrostimulation.

**Gültuna I.**

Interprofessional Pain Care symposium 12-sept-2015 Amsterdam

Improve Patient's safety perioperatively.

**Koopman-van Gemert A.W.M.M.**, Dekker van Doorn C.M., Wauben L.S.G.L.. BIT's 2nd Annual World Congress of Orthopedics.  
24-26 september 2015 te Xi'an China

Radiofrequency in pain medicine.

**Gültuna I..**

St Jude Medical training 01-okt-2015 Veenendaal

Radiofrequency treatments in Chronic pain medicine.

**Gültuna I.**

Pain Workshop 02-okt-2015 Gent

Discussietafel patientveiligheid.

**Koopman-van Gemert A.W.M.M.**

Congres Patientveiligheid 7 oktober 2015 Eenhoorn Amersfoort.

Nieuwe richtlijn Neuraxisblokkade en Antistolling van de NVA.

**Koopman-van Gemert A.W.M.M.**

Applicatiecursus Federatie Nederlandse Trombosedienst 8 oktober 2015 te Bilderberg hotel de Klepperman te Hoevelaken

Nieuwe richtlijn Neuraxisblokkade en Antistolling van de NVA.

**Koopman-van Gemert A.W.M.M.**

Applicatiecursus Federatie Nederlandse Trombosedienst 5 november 2015 te Bilderberg hotel de Klepperman te Hoevelaken

Nieuwe anticoagulantia (NOACs) en de actuele status van de richtlijn Neuraxisblokkade en Antistolling.

**Koopman-van Gemert A.W.M.M.**

NVA-cursus 9 november 2015 Fletcher Hotel Doorwerth Arnhem

Wat is pijn?

**Gültuna I.**

Vereniging Pijn Patiënten 02-dec-2015 Dordrecht

Workshops Patientveiligheid Canbetter. Haming J.J.

**Koopman-van Gemert A.W.M.M.**, Den Rooyen C.

MMV congres 9 december 2015 te Nieuwegein.

Bloed- en (anti)stollingsbeleid op de poli.

**Koopman-van Gemert A.W.M.M..**

4e Christmas Stollings Symposium 18 december 2015 AMC te Amsterdam

### Posters op geaccrediteerde wetenschappelijke congressen

Improvement sepsis outcome in a large hospital organisation: Take your time and invite other professions to help you.

Oskam E, Ponssen H.H., Gent A.J. van, **So KL**.

International Forum on Safety and Quality in Healthcare.

22 april 2015 London, Engeland

The impact of implementing a rapid response system: a comparison of cardiopulmonary arrests and mortality among two clinical locations of a large teaching hospital in the Netherlands.

Jonker-Ruitenbeek H., Doorn van J., Nadort van L., Klei van der D., Jansen W.J., Ponssen H.H., **So KL**.

11th Int Congress on Rapid Response Teams and Medical Emergency Teams.

18-19 mei 2015. Amsterdam

Barriers to activate the rapid response system: an analysis of professional resistance, safety culture and teamwork.

Goutier J.M., Jansen W.J., **So KL**

11th Int Congress on Rapid Response Teams and Medical Emergency Teams.

18-19 mei 2015 Amsterdam

The effect of early identification of and response to clinically deteriorating patients on the surgical ward by using automated continuous patient monitoring on mortality: is there a "weekend effect"?

**So KL**, Jansen W., Schilp J. Plaisier P., Wagner C.

11th Int Congress on Rapid Response Teams and Medical Emergency Teams.

18-19 mei 2015 Amsterdam (nominatie posterprijs)

Perioperatieve Transfusion Study (PETS): does a liberal transfusion protocol improve outcome in high-risk cardiovascular patients undergoing non-cardiac surgery?

**Ali S, Koopman-van Gemert AWMM**, Lijkwan M.A., Stolker R.J., Lier van F.

Wetenschapsdag ASz, 18 juni 2015.

Auditorium ASz Dordrecht

Mini-audit of the afferent limb of rapid response system: an evaluation of nursing practice on surgical and medical patients during both weekdays and weekends.

Hoor van A., Jansen W.J., **So K.L.**

Wetenschapsdag ASz, 18 juni 2015.

Auditorium ASz Dordrecht

The impact of implementing a rapid response system: a comparison of cardiopulmonary arrests and mortality among two clinical locations of a large teaching hospital in the Netherlands.

Jonker-Ruitenbeek H., Kleij van der D., Doorn van J., Nadort L. van, Jansen W.J., Ponssen H.H., **So K.L.**

Wetenschapsdag ASz, 18 juni 2015.

Auditorium ASz Dordrecht

The role of fibrinogen in massive postpartum hemorrhage, a case report.  
Minde M.R.C. van, **Koopman-van Gemert A.W.M.M.**, Rombout-de Weerd S.  
Wetenschapsdag ASz, 18 juni 2015.  
Auditorium ASz Dordrecht.

Remifentanyl use for procedural sedation and analgesia in the emergency department.  
Hooft M.A.A. van, America R., Oskam E., **Koopman-van Gemert A.W.M.M.**  
Wetenschapsdag ASz, 18 juni 2015.  
Auditorium ASz Dordrecht

Improvement sepsis outcome in a large hospital organisation: Take your time and invite other professions to help you.  
Oskam E, Ponsen H.H., Gent A.J. van, **So K.L.**  
Wetenschapsdag ASz, 18 juni 2015.  
Auditorium ASz Dordrecht

The effect of early identification of and response to clinically deteriorating patients on the surgical ward by using automated continuous patient monitoring on mortality: is there a "weekend effect" ?  
**So K.L.**, Jansen W., Schilp J. Plaisier P., Wagner C.  
Wetenschapsdag ASz, 18 juni 2015.  
Auditorium ASz Dordrecht

Long term outcome of subcutaneous stimulation as an additional therapy to Spinal Cord Stimulation for the treatment of low back and leg pain in patients with Failed Back Surgery Syndrome.  
**T.E.Hamm-Faber MA-ANP, J.A.Aukes MD, E.J.J.A.A. van Gorp MD, I.Gültuna MD.**  
"10 June 2015 World congress INS (International Neuromodulation Society) Montreal, Canada

Subcutaneous stimulation as ADD-ON therapy to SCS is effective in treating low back pain in patients with Failed Back Surgery Syndrome: a multicenter randomized controlled trial.  
**E.J.J.A.A. Gorp**, K.Burger, R.Schapendonk, J.Kallewaard, G.Spincemaile, T.Hamm, L. vonhogen Jan, CM.Hendriks, Kris.Vissers.  
10 June 2015 World congress INS (International Neuromodulation Society) Montreal, Canada

# Cardiologie

## Voordrachten op geaccrediteerde wetenschappelijke congressen

Cardiomyopathie: definitie, classificatie, prognose en beeldvorming middels echo en MRI.

**Kofflard M.J.M.**

Echoavond Albert Schweitzer ziekenhuis, Dordrecht 19 feb 2015.

Accreditatie: 2 uur.

SEH congres 26 en 27 maart, Albert Schweitzer ziekenhuis, Dordrecht

Op 26 maart: dagvoorzitter **Kofflard M.J.M.**. 26 maart voordracht: workshop HOCM

Kofflard M.J.M.

27 maart voordracht: workshop HOCM.

Accreditatie: 14 uur voor cardiologen.

Bijzondere echobeelden uit de periferie.

**Gent van M.W.F., Kofflard M.J.M.**

Echoavond Albert Schweitzer ziekenhuis, Dordrecht, 16 april 2015.

Accreditatie: 2 uur.

De betekenis van MRI bij de patient met een hypertrofische cardiomyopathie

**Kofflard M.J.M.**

Voordracht op Lustrum symposium Cardiologenclub Rijnmond, "De Rotterdam", 26 juni 2015.

Accreditatie symposium: 3 uur.

Casuïstiek uit de periferie.

**Bos van der E.J., Kofflard M.J.M.**

Echoavond Albert Schweitzer ziekenhuis, Dordrecht 12 november 2015

Accreditatie: 2 uur.

Echoavond Albert Schweitzer ziekenhuis, Dordrecht.

Differentiaal diagnostiek van linker ventrikel hypertrofie.

Dr. Michels, **Kofflard M.J.M.** Dordrecht. 3 december 2015.

Accreditatie: 2 uur.

TCT-419 Upper Extremity Dysfunction Post Transradial Percutaneous Coronary Intervention; Interim results

Eva Zwaan, Carlo A. Holtzer, **Marcel J. Kofflard** and Alexander J. IJsselmuiden

J Am Coll Cardiol. 2015;66(15\_S):.

N-terminal pro brain natriuretic peptide (NT-proBNP) correlates with echocardiographic signs of cardiotoxicity during Her2Neu-receptor blocking therapy in patients with Her2Neu-positive breast cancer.

Liesting C, Brugts JJ, **Kofflard MJM**, Sprangers S, Fouraux M, Cramer GE, Kitzen JJEM, de Rooi JJ, Boersma E, Levin M-D.

Neth Heart J 2015;23:Suppl:21

Myocardial edema assessed with T2-weighted CMR imaging is associated with adverse clinical features in hypertrophic cardiomyopathy.

Gommans DHF, Cramer GE, Bakker J, Michels M, Dieker HJ, Fouraux MA, Marcelis CLM, Timmermans J, Brouwer MA, **Kofflard MJM**.

European Society Cardiology congress. 2015, Londen.

ECG-diagnostiek, een risico? ECG-diagnostiek in de cardiovasculaire risicoschatting in de huisartsenpraktijk

**Ijsselmuiden**

Cordiaal, 2015

First-in-man evaluation of the novel balloon delivery system STENTYS Xposition S for the self-apposing coronary artery stent: impact on longitudinal geographic miss during stenting

**Ijsselmuiden**, Vries de, Weevers, Scholte

Eurointervention, 2015

Een onderzoek naar de veiligheid en toepasbaarheid van de Drug Eluting Balloon (DEB) - De PEARL trial

**Driel van A.G.**

Cordiaal en WASz, 2015

OpenII result from 6 and 12 months

**Ijsselmuiden**

Eurointervention, 2015

### Abstracts en posters

First-in-man (FIM) evaluation of a novel balloon delivery system for the self-apposing coronary artery stent - 30 days results

**Ijsselmuiden**, Weevers, Scholte, de Vries

EuroPCR, 2015

EuroPCR presentatie ABSORB First

**Ijsselmuiden**, Weevers, Scholte, Vries de

EuroPCR, 2015

The clinical outcomes at 24 months of the OPEN II study

**Ijsselmuiden**

EuroPCR, 2015

30 dagen resultaten van de PEARL

**Driel van A.G.**

Wetenschapsdag 2015, Asz

End-of life management bij ICD patiënten

**Driel van A.G.**

Wetenschapsdag 2015, Asz

Upper Extremity Dysfunction Post Transradial Percutaneous Coronary Intervention; Interim results  
Zwaan, **IJsselmuiden**  
TCT, 2015

30-Days interim results of a new paclitaxel coated drug eluting balloon (DEB) in real-world  
PCI indications  
**Driel van A.G., IJsselmuiden**  
TCT, 2015

Long term results of a Self-Apposing Bare Metal versus Paclitaxel-Eluting Coronary Stent for  
the treatment of Saphenous Vein Grafts  
Driel van A.G., **IJsselmuiden**  
TCT, 2015

An ostial lesion of a large estatic right coronary artery treated by a large self-apposing stent  
via a new balloon delivery system  
Jong-Salentijn, **IJsselmuiden**  
TCT, 2015

N-terminal pro brain natriuretic peptide (NT-proBNP) correlates with echocardiographic signs  
of cardiotoxicity during Her2Neu-receptor blocking therapy in patients with Her2Neu-positive  
breast cancer  
**Kofflard MJM**  
Neth Heart J, 2015; 23 suppl: 21

#### **Internet publicaties**

Absorb first – newsletter edition #12, april 2015  
**IJsselmuiden**  
EuroPCR, 2015

# Chirurgie

## Overige publicaties

Short-term morbidity and quality of life from a randomized clinical trial of close rectal dissection and total mesorectal excision in ileal pouch-anal anastomosis.

**Bartels SAL**, Gardenbroek TJ, Aerts M, et al.

Br J Surg 2015;102:281-7. doi: 10.1002/bjs.9701

Ulnarisletsel bij een ongecompliceerde antebrachiumfractuur.

**Bul M, Jakma TSC.**

Ned Tijdschr Traumachir 2015;23:37.

Heupfracturen bij kinderen

**Van der Ende B, Jakma TSC.**

Ned Tijdschr Traumachir 2015;23:2-6.

Severe wear and pseudotumor formation due to taper mismatch in a total hip arthroplasty: a case report.

**Koper MC**, Matthijsen NMC, Witt F, Morlock MM, Vehmeijer SBW.

JBJS Cas Connect 2015;5:e29. doi: 10.2106/JBJS.CC.N.00104

Repositie van supracondylaire humerusfracturen middels een tijdelijke Kirschner-draad.

**Moerman S, Buisman FE, Schütte PR, Punt BJ.**

Ned Tijdschr Traumachir 2015;23:32-6.

Wikileaks treft Nederlandse chirurgen op congres in VS: over de rol van de schildwachtklierprocedure bij het melanoom.

**Plaisier PW**, de Wilt JHW.

Ned Tijdschr Heelkd 2015;24:10-11.

Vroeger was chirurgie nog leuk... (of : een tamelijk kritische 'appraisal' van de richtlijn 'appendicitis').

**Plaisier PW.**

Memorad 2015; 20 :19-20.

Photodynamic bone stabilization system: the next step.

**Vegt PA.**

Ned Tijdschr Trauma 2015;23:86-92.

Marking axillary lymph nodes with radioactive iodine seeds for axillary staging after neoadjuvant systemic treatment in breast cancer patients: the MARI procedure.

Donker M, Straver ME, Wesseling J, Loo CE, Schot M, **Drukker CA**, van Tinteren H, Sonke GS, Rutgers EJ, Vrancken Peeters MJ.

Ann Surg 2015;261:378-82. doi: 10.1097/SLA.0000000000000558.

Tropenartsen in vervolgopleiding tot chirurg: dubbel winst?

Gordinou de Gouberville M, **Reuling E**.

Ned Tijdschr Heelkd 2015;24:12-3.

Reply to "Can we avoid rectus abdominis muscle atrophy and midline shift after colostomy creation?"

Timmermans L, Deerenberg EB, van Dijk SM, **Lamme B**, Koning AH, Kleinrensink GJ, Jeekel J, Lange JF.

Surgery 2015;157:179-180. Doi: 10.1016/j.surg.2014.09.021.

Multiparametric MRI With Dynamic Contrast Enhancement, Diffusion-Weighted Imaging, and <sup>31</sup>P-Phosphorus Spectroscopy at 7 T for Characterization of Breast Cancer.

Schmitz AM, Veldhuis WB, **Menke-Pluijmers MB**, van der Kemp WJ, van der Velden TA, Kock MC, Westenend PJ, Klomp DW, Gilhuijs KG.

Invest Radiol. 2015;50:766-71.

Effect of a ward-based pharmacy team on preventable adverse drug events in surgical patients (SUREPILL study).

Surgery and Pharmacy in Liaison (SUREPILL) Study Group (**Oostenbroek RJ**).

Br J Surg 2015;102:1204-12. DOI: 10.1002/bjs.9876.

### **Boek of hoofdstuk in boek**

The Pirogoff Amputation. In: Alexander IJ, Bluman EM, Greisberg JK. Advanced Reconstruction: Foot and Ankle II.

Langeveld ARJ, Meuffels DE, **Hoedt MTC**

Rosemont (IL), USA, American Academy of Orthopedic Surgeons; 2015.

### **Voordrachten op geaccrediteerde wetenschappelijke congressen**

Gene signature for risk stratification and treatment of breast cancer: incorporating tumor biology in clinical decision-making.

**Drukker CA.**

Najaarsvergadering, November 2015.

Geaccrediteerd door Nederlandse Vereniging voor Heelkunde.

Wrist fractures treated with a new percutaneous intramedullary rod osteosynthesis:

IlluminOss® using a polymerized monomer – a Case Series.

**Klitsie PJ.**

16th European Congress of the European Society for Trauma & Emergency Surgery, Amsterdam, Mei 2015.

Geaccrediteerd door the European Society for Trauma & Emergency Surgery

IlluminOss® is a new percutaneous intramedullary rod osteosynthesis using a polymerized monomer – A case series on patients with wrist fractures

**Klitsie PJ.**

Annual Küntscher Meeting, Brussel, September 2015.

Geaccrediteerd door Osteosynthese International

Vooral problemen op het gebied van communicatie en medisch handelen leiden tot klachtenprocedures: 5 jaar formele klachtenprocedures in een opleidingsziekenhuis.

**Oostenbroek RJ, Plaisier PW.**

NVMO congres 2015, November 2015, Rotterdam.

Geaccrediteerd door Nederlandse Vereniging voor Medisch Onderwijs

Mastectomie bij bewezen DCIS/mammacarcinoom en uitgebreide laesie op MRI .

**Menke-Pluijmers MBE**

14<sup>e</sup> AvL mammasymposium, Oktober 2015, Amsterdam.

Geaccrediteerd door Nederlandse Vereniging voor Heelkunde.

### Posters op geaccrediteerde wetenschappelijke congressen

Agreement in risk assessment among breast cancer specialists: A survey within the MINDACT cohort.

**Drukker CA.**

IMPAKT Breast Cancer Conference 2015, Mei 2015, Brussel.

Compartment Syndrome of the Foot: Current concepts of diagnosis and treatment in relation to a rare case of acute onset.

**Hoedt M, Jakma TSC, Reitsma M.**

16th European Congress of the European Society for Trauma & Emergency Surgery, Mei 2015, Amsterdam.

Moet iedere in opzet curatief geopereerde mammacarcinoompatiënt worden besproken met een consulent?

**Plaisier PW, Teune TM, Geel van AN.**

13e Bossche Mamma Congres, Juni 2015, Sint Michielsgestel.

Heeft hyperbare zuurstoftherapie toekomst bij de behandeling van late radiatieschade?

Geel van AN, Poortmans P, Koppert LB, **Plaisier PW**, Struikmans H, van der Rijt CCD, et al.

13e Bossche Mamma Congres, Juni 2015, Sint Michielsgestel.

The effect of early identification of and response to clinically deteriorating patients on the surgical ward by using automated continuous patient monitoring on mortality: is there a "weekend effect" ?

So RKL, Jansen WJ, Schilp J, **Plaisier PW**, Wagner C.

11th International Conference on Rapid Response Systems and Medical Emergency Teams, Mei 2015, Amsterdam.

### Proefschriften

*"Basic research in cardiovascular disease: from stem cells to immunomodulation."*

**Lijkwan, MA**

Rijks Universiteit Leiden

Promotor : Prof. dr J.F. Hamming en Prof. dr P.H.A. Quax

18 juni 2015

*"Tailored treatment of metastatic colorectal cancer: clinical and pre-clinical developments."*

**Kuijpers AMJ**

Universiteit van Amsterdam

Promotor : Prof. dr E.J.Th. Rutgers

30 september 2015

# Dermatologie

## Overige publicaties

(Pre)malignant disorders of the oral cavity. In Handboek dermatologische oncologie.

**Laeijendecker R.** (Pre)maligne afwijkingen van de mondholte.[Dutch].

Onder redactie van Beljaards RJ, Neumann HAM, Bergman W, 2015, 167-79, 383. ISBN-EAN: 978-94-90826-40-6.

# Gynaecologie

## Overige publicaties

The role of fibrinogen in massive postpartum haemorrhage, a case report  
Minde van MRC\*, Koopman-van Gemert AWMM, Rombout – de Weerd S.  
Case Reports in Women's Health 6 (2015) 4–5

# Interne Geneeskunde

## Overige publicaties

"Uw diagnose?"

Heul van der-Nieuwenhuijsen L, **Levin MD**, Ngyen BD, Nederveen van FH, Vermeer HJ, Riedl J  
NTvH 2015;12:75-76

"MURANO-studie: venetoclax voor patiënten met recidief of refractaire CLL"

Kater AP, **Levin MD**, Kersting S, Chamuleau M, Lugtenburg P, Nijland M, de Weerd O, Veelken H, Raymakers R, van Kampen R, Regelink J, Nijziel M, Leys R, Schaafsma R NTvH 2015;12:100-103

Anafylactoïde reactie op acetylcysteïne na een paracetamol intoxicatie: staken of doorbehandelen

Schoenmakers R, Beex M., Ponssen HH, Dieleman H., Tijssen G.  
Pharmacotherapeutisch Weekblad, wetenschappelijk platform, 2015; 9: A, 1530

## Voordrachten

Omitting Cytogenetic Response Assessment and Using Only Molecular Response Assessment to TKI Treatment in CML is Safe and Prevents Misclassification As Treatment Failure.

Geelen GP, Thielen N., Janssen JJ, Roosma T., Visser O, Valk PJM, Cornelissen JJ, **Westerweel PE**

"Oral presentation" op "the 17th Annual John Goldman Conference on Chronic Myeloid Leukemia: Biology and Therapy" op Oktober 1-4, 2015 – Estoril, Portugal (abstract).

"Survival of patients with Her2 positive metastatic breast cancer after failure of adjuvant treatment with Trastuzumab"

**Rier HN**, Hooning M., Jager A, Kitzen JJEM, Sleijffer S., Levin M-D.  
27ste Internistendagen, Maastricht.

"Inleiding op CML, huidige richtlijnen en lopende studies".

**Westerweel PE**

CML Masterclass, Dordrecht, 8 januari 2015

"De deur open naar de digitale spreekkamer".

**Westerweel PE**

Lustrumsymposium Politheek Albert Schweitzer Ziekenhuis, Dordrecht, 20 januari 2015

"An overview of CML research in the Netherlands".

**Westerweel PE**

European Investigators in CML meeting, 8 maart 2015, Bologna, Italië

"Nieuwe CML studies".

**Westerweel PE**

Regionale hematologiebijeenkomst, Erasmus MC, 12 maart 2015

"Proposed novel studies in CML"

**Westerweel PE**

HOVON/ SAKK Leukemia Meeting, Schiphol, 18 maart 2015

"A case of de novo CML in accelerated / blast phase"

**Westerweel PE**

CML preceptorship, Hammersmith hospital, Londen, UK.

"Therapietrouw bij CML en de potentie van e-health"

**Westerweel PE**

Symposium "Therapietrouw bij het gebruik van orale oncolytica" VU Medisch centrum, 22 juni 2015

"Sports diving with anticoagulation: possibilities and limitations"

**Westerweel PE**

41e Congress of the European Underwater and Baromedical Society, 19-22 Augustus, Amsterdam 2015.

"NOACs in de klinische praktijk: een praktisch ABC"

**Westerweel PE**

Satellietsymposium annual meeting van de European Respiratory Society, Amsterdam, 28 September 2015

"Plussen en minnen in de MPN. Hoe krijg je de Ph- MPN positief en de Ph+ MPN negatief?"

**Westerweel PE**

Klinische dag Nederlandse Vereniging voor Hematologie. Utrecht, 5 november 2015

"Duiken met bloedverdunners".

**Westerweel PE**

Veilig duiken symposium, Dordrecht, 7 november 2015

"Chronische Myeloïde Leukemie (CML). Nieuwe inzichten in diagnostiek en behandeling"

**Westerweel PE**

State-of-the-art lezing op thema-avond CML van het Radboudumc, Nijmegen, 23 november 2015.

**Poster**

Rituximab-Pecc Induction Followed By 90y-Ibritumomab Tiuxetan Consolidation in Relapsed or Refractory DLBCL Patients Who Are Not Eligible for or Have Failed ASCT: Results from a Phase II HOVON Study

**Berenschot HWA**; balanced scorecard hemato-oncologie

'Health-related Quality of Life and Patient-reported Outcomes in Patients Receiving Ofatumumab Maintenance Versus Observation in the PROLONG Trial"

Oers van M, Kuliczkowski K., Smolej L., Petrini M., Offner F., Grosicki S, **Levin M-D**, Gupta I., Phillips J., Williams V, Manson S, Lisby S, Geisler C.

20th EHA congres, Wenen, Oostenrijk.

"Health-related Quality of Life and Patient-reported Outcomes in Patients Receiving Ofatumumab Maintenance Versus Observation in the PROLONG Trial"

Oers van M., Kuliczkowski K., Smolej L., Petrini M., Offner F., Grosicki S., **Levin M-D**, Gupta I., Phillips L., Williams V., Manson S., Lisby S., Geisler C..

16th International Workshop on Chronic Lymphatic Leukemia, Sydney, Australie

"Multi-center randomized open label phase II trial on 3 rituximab dosing schemes in immune thrombocytopenia patients"

Zwaginga JJ, van der Holt B, Boekhorst te PA, Biemond BJ, **Levin MD**, Griend van der R, Brand A, Zweegman S, Pruijt HF, Novotny VM, Vreugdenhil A, de Groot MR, de Weerd O, Pampus van EC, Maanen van-Lamme TM, Wittebol S, Schipperus MR, Silbermann MH, Huijgens PC, Luten M, Hollestein R, Brakenhoff JA, Schrama JG, Valster FA, Velders GA, Koene HR.

Haematologica 2015 mar; 100 (3); e90-e92.

Examination of peripheral blood smears: performance evaluation of a digital microscope system using a large-scale leukocyte database"

Stouten K, Riedl JA, **Levin MD**, Gelder van W.

Int J Lab Hematol, 2015 Jun 8 (Epub ahead of print)

Richtlijn voor diagnostiek en behandeling van chronisch lymfatische leukemie / kleincellig lymfocytair lymfoom"

Kersting S, Levin M-D, Chamuleau M., et. al.

NTvH 2015; 12: 205-216

Ofatumumab maintenance versus observation in relapsed chronic lymphocytic leukaemia (PROLONG): an open-label, multicentre, randomised phase 3 study"

Oers van MH, Kuliczkowski K, Smolej L, Petrini M, Offner F, Grosicki S, **Levin MD**, Gupta I, Phillips J, Williams V, Manson S, Lisby S, Geisler C; PROLONG study investigators

Lancet Oncol. 2015 Oct;16(13):1370-9.

# Kindergeneeskunde

## Overige publicaties

Is Rapydan® pleister superieur aan Emla® crème als lokaal anestheticum bij kinderen?

Een systematische review.

Erkelens JRS, **Welborn KM**, Beex-Oosterhuis MM.

Korte bijdrage - Wetenschappelijk platform - Pharmaceutisch Weekblad

Steeds meer specialisten gebruiken WhatsApp. Richtlijnen nodig voor gebruik van moderne communicatiemiddelen.

**Wiggelinkhuizen M.**, Hendriks MS, Hoog de M, **Sas TCJ**

Medisch Contact 26 november 2015, blz 2310-2311.

## Mondelinge voordrachten

Transdermal low dose estrogens in girls with Turner syndrome – update.

**Sas TCJ**, Ankarberg-Lindgren C.

Oral presentation. Turner Working Group Symposium, ESPE oktober 2015, Barcelona.

Puberteitsinductie.

**Sas TCJ**

Werkgroep kinder- en adolescentengynaecologie van o.a. de NVK 14 oktober 2015, Utrecht

Ontslag naar huis met voeding (deels) via sonde bij prematuren < 37 weken. Nieuwe standaard?

**Stoelhorst GMSJ**

Vlaams Nederlandse Neonatologendag, 12 juni jl in Antwerpen.

Deze presentatie ook tijdens NVK 2015 (woensdag 4 november)

IGF-I and growth in early childhood in VLBW infants versus term born infants

**Jong de M**

Gepresenteerd op de '54th Annual meeting of the European Society for Paediatric Endocrinology'

Okt 2015, Barcelona

## Poster presentaties

E-mail & WhatsApp: Bedreiging patiëntgegevens. Inventarisatie gebruik E-mail, WhatsApp en privé-telefoon door specialisten op de werkvloer

M.S. Hendriks, **Wiggelinkhuizen M**, **Sas TCJ**

Posterpresentatie ASz wetenschapsdag 18 juni 2015:

Is rapydan® superieur aan EMLA® als lokaal anestheticum bij kinderen?

J.R.S. Erkelens, **Welborn KM**, M.M. Beex-Oosterhuis

Poster wetenschapsdag ASz 18 juni 2015:

Ontslag naar huis met voeding (deels) via sonde bij prematuren < 37 weken. Nieuwe standaard?

**Kampen van F, Lege de-Korstanje J, Mol de A, Stoelhorst GMSJ**

Mondelinge presentatie tijdens wetenschapsdag ASz 18 juni 2015

Ontslag naar huis met voeding (deels) via sonde bij prematuren < 37 weken. Nieuwe standaard?

**F van Kampen, J de Lege-Korstanje, A De Mol en GMSJ Stoelhorst**

Vlaams Nederlandse Neonatologendag gehouden op 12 juni jl in Antwerpen.

# Leerhuis

## Invited lectures and presentations:

Barriers in the process of giving and receiving feedback

**Ridder van de JMM**

International Clinical Educators Network Summit, Glasgow, Scotland, September 10, 2015

## Paper and poster presentations, workshops, abstracts, and colloquy:

Barriers in the feedback process [Barrières in het feedback proces]

**Ridder van de JMM**

KNMG, Nieuwegein, the Netherlands, December 9, 2015.

Workshop presented at Modernising Medische Vervolgopleiding Conference

Barriers in the feedback process [Barrières in het feedback proces]

**Ridder van de JMM**

Workshop presented at NVMO Group Medical Education in Practice, Utrecht, the Netherlands, September 23, 2015.

Barriers in the feedback process [Barrières in het feedback proces]

**Ridder van de JMM**

Workshop presented at OOR-ZWN symposium, Tilburg, the Netherlands, September 19, 2015.

Barriers in the feedback process: theory and practice

**Ridder van de JMM**

Presentation at Symposium Advances in health professions education research and development: 10 years Expertise Centrum UMC Utrecht, Utrecht, the Netherlands, September 11, 2015.

Residents' participation in a system of educational quality management

Oostenbroek R, **Ridder van de JMM**

Poster presented at the Association for Medical Education in Europe 2015 Conference, Glasgow, Scotland, September 5th - September 9th, 2015.

Conference Workshop: How to give negative feedback in medical education – Conceptual issues & best practices.

Fabry G, Goerlitz A, Kiessling C, **Ridder van de JMM**

Workshop presented at the Association for Medical Education in Europe 2015 Conference, Glasgow, Scotland, September 5th - September 9th, 2015.

What is the relationship between feedback preference and self-efficacy in communication tasks?

Huiden EM, Grosfeld FJM, Willemsen S, **Ridder van de JMM**

Paper presented at the Association for Medical Education in Europe 2015 Conference, Glasgow, Scotland, September 5th - September 9th, 2015.

Conference Workshop: Young medical educators' workshop: Finding the right mentor in Medical Education.

Huwendiek S, Mennin S, Ringsted C, Amin Z, **Ridder van de JMM**

Workshop presented at the Association for Medical Education in Europe 2015 Conference, Glasgow, Scotland, September 5th - September 9th, 2015.

Feedback seeking: Giving feedback to the activated learner.

**Ridder van de JMM**, Blatt B, Kachur EK, Capello C, Verhoeven B

Pre-conference workshop presented at the Association for Medical Education in Europe 2015 Conference, Glasgow, Scotland, September 5th - September 9th, 2015.

Culture matters: Feedback in health profession education for diverse learners in international settings.

Dong D, Tan C-H, Kachur E, Lin T, **Ridder van de JMM**

Pre-conference workshop presented at the Association for Medical Education in Europe 2015 Conference, Glasgow, Scotland, September 5th - September 9th, 2015.

Identifying limiting and promoting factors for interprofessional education (IPE) within the field of Medical Education: the Dutch experience.

Vries-Erich IM, Veenhoven H, Maaijer P de, Reuchlin C. **Ridder van de JMM**

Paper presented at the 5th European conference on International Practice and Education, Nijmegen, the Netherlands, August 25-28, 2015.

Feedback in clinical education: a lay presentation.

**Ridder van de JMM**

Presentation on Symposium Feedback in Clinical Education. Albert Schweitzer hospital, Dordrecht, The Netherlands, July 3rd 2015.

Addressing and agreeing: Feedback giving techniques for advanced. [Aanspreken en afspreken: Feedback geven voor gevorderden].

**Ridder van de JMM**, van der Meulen Y

Symposium OOR-Leiden, Den Haag, The Netherlands, April 14, 2015

# Longgeneeskunde

## Poster presentatie

**Vincenten J.**

Wereld Longkanker congres Denver

# Maag-, Darm- en Levergeneeskunde

Gastroenterology

**Alderliesten J.**

2015 Mar 17. pii: S0016-5085(15)00346-7. doi: 10.1053/j.gastro.2015.03.012.

[Epub ahead of print]

# Neurologie

The Negative Predictive Value of the Head Impulse Test, Nystagmus, and Test of Skew Deviation Bedside Oculomotor Examination in Acute Vestibular Syndrome.

Venhovens J, Meulstee J, Verhagen WI.

Ann Emerg Med. 2015 Jul;66(1):91-2. doi: 10.1016/j.annemergmed.2015.03.009. No abstract available.

Vestibular evoked myogenic potentials (VEMPs) in central neurological disorders.

Venhovens J, Meulstee J, Verhagen WI.

Clin Neurophysiol. 2015 Jan 16. pii: S1388-2457(15)00011-5. doi: 10.1016/j.clinph.2014.12.021. [Epub ahead of print]

Preventive antibiotic therapy in stroke: PASSed away?

The Lancet, January 2015

# Ouderengeneeskunde

Testing Van Gool's Hypothesis: A Method to Predict Side Effects of Cholinesterase Inhibitors in Patients with Cellular Degenerative and Vascular Dementia

**Groot ER**

Advances in Geriatrics, vol. 2015, Article ID 270657, 6 pages, 2015.

doi:10.1155/2015/270657.

# Pathologie

## Boek

The orbit including the lacrimal gland and lacrimal drainage system.

Verdijk RM, Pecorella I, **Mooy CM**

Eye pathology: an illustrated guide. Heegaards S, Grossniklaus H (Eds) Springer-Verlag Berlin 2015. Chapter 12

## Abstracts

### **Multidisciplinary breast cancer registry: improvement of quality of care through the NABON Breast Cancer Audit**

Siesling, Comprehensive Cancer Centre the Netherlands (IKNL), Utrecht, the Netherlands / University of Twente, Enschede, the Netherlands

- Annelotte C. van Bommel, Leiden University Medical Centre, Leiden, the Netherlands
- Marie-Jeanne T. Baas - Vrancken Peeters, Netherlands Cancer Institute / Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands
- Margriet van der Heiden- van der Loo, Netherlands Comprehensive Cancer Centre Organisation (IKNL), Utrecht, the Netherlands
- Michel W. Wouters, Netherlands Cancer Institute / Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands
- Marc Lobbes, Maastricht University Medical Centre, Maastricht, the Netherlands
- Ruud M. Pijnappel, University Medical Centre Utrecht, Utrecht, the Netherlands
- Marc A. Mureau, Erasmus MC Cancer Institute, Rotterdam, the Netherlands
- **Pieter J. Westenend**, Laboratory for pathology Dordrecht e.o., Dordrecht, the Netherlands
- Kay Schreuder, Netherlands Comprehensive Cancer Centre Organisation (IKNL), Utrecht, the Netherlands
- Pauline Spronk, Dutch Institute for Clinical Auditing (DICA), Leiden, the Netherlands
- Bart de Vries, Maastricht University Medical Centre, Maastricht, the Netherlands
- Carolien H. Smorenburg, Netherlands Cancer Institute / Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands
- Agnes Jager, Erasmus MC Cancer Institute, Rotterdam, the Netherlands
- John H. Maduro, University Medical Centre Groningen, Groningen, the Netherlands
- Henk Struikmans, MCH Westeinde, the Hague, the Netherlands
- Carol Richel, Dutch Breast Cancer Association, Utrecht, the Netherlands
- Marga Schrieks, Dutch Breast Cancer Association, Utrecht, the Netherlands
- Maïke Schepens, Health Insurer Netherlands
- Thijs van Dalen, Diaconessenhuis Utrecht, Utrecht, the Netherlands
- European congress of epidemiology, Maastricht 2015

7T Breast MRI to Visualize Proliferative Characteristics of Breast Cancer using DCE, DWI, and 31P-MRS.

Schmitz AMTh, Veldhuis WB, Menke-Pluijmers MBE, Kemp van der WJM, Velden van der TA, Kock MCJM, **Westenend PJ**, Klomp DWJ, Gilhuijs KGA

International Society for Magnetic Resonance in Medicine, Toronto 2015

Multi-parametric DCE-MRI, DWI, and 31P-MRS at 7 Tesla for preoperative indication of chemotherapy in patients with early breast cancer  
Schmitz AMTh, Veldhuis WB, Menke-Pluijmers MBE, Kemp van der WJM, Velden van der TA, Kock MCJM, **Westenend PJ**, Klomp DWJ, Gilhuijs KGA  
Radiology Society of the Netherlands, Rotterdam 2015

Multi-parametric MR Imaging at 7 Tesla for preoperative indication of chemotherapy in patients with early breast cancer  
Schmitz AMTh, Veldhuis WB, Menke-Pluijmers MBE, Kemp van der WJM, Velden van der TA, Kock MCJM, **Westenend PJ**, Klomp DWJ, Gilhuijs KGA  
Radiology Society of North America, Chicago 2015.

Underestimate rates and upgrading in patients with a needle biopsy diagnosis DCIS in the Netherlands  
**Meurs CJC**<sup>1</sup>, Heiden van der- van der Loo van der M.<sup>2</sup>, Menke – Pluijmers MBE<sup>3</sup>, Overbeek LIH<sup>4</sup>, **Westenend PJ**  
NVVP Pathologendagen, Ede 2015

Use of the sentinel node biopsy for patients with a needle biopsy diagnosis DCIS in the Netherlands  
**Meurs CJC**<sup>1</sup>, Heiden van der-Loo van der M<sup>2</sup>, Menke – Pluijmers MBE<sup>3</sup>, Overbeek LIH<sup>4</sup>, **Westenend PJ**<sup>5</sup>  
Bossche mammadagen 2015

### Voordrachten

Use of the sentinel node biopsy for patients with a needle biopsy diagnosis DCIS in the Netherlands.  
**Westenend PJ**  
Bossche mammadagen 2015

Praktijkvariatie: diagnostiek bij ductal carcinoma in situ.  
**Meurs CJC**  
NVVP, Lent 2015

Is de aanwezigheid van een invasief carcinoom na een biopsie diagnose met DCIS voorspelbaar?  
**Westenend PJ**  
Symposium Behandeling Borstkanker Beter, Rotterdam 2015

# Radiologie

## Overige publicaties

Ischemic cardiomyopathy and cerebral infarction in a young patient associated with khat chewing.  
Meulman TJ, **Bakker J**, van den Bos EJ.  
Case Rep Radiol. 2015;2015:893176.

Heme-induced acute kidney injury following hemolysis after thermal ablation of symptomatic giant hepatic hemangiomas: a report of two cases.  
**Aukje A.J.M. van Tilborg**, Helena F. Dresselaars, Hester J. Scheffer, Colin Sietses, Petrousjka M. van den Tol, Martijn R. Meijerink  
Clin Radiol. *Submitted*.

Transcatheter CT hepatic arteriography (CTHA) guided percutaneous ablation to treat ablation site recurrences of colorectal liver metastases: the incomplete ring sign  
**van Tilborg AAJM**, Scheffer HJ, van der Meijs BB, van Werkum MH, Melenhorst MCAM, van den Tol MP, Meijerink MR. J  
Vasc Interv Radiol. 2015 Apr;26(4):583-587

A curly case: dissecting giant arteriovenous anomaly - left main coronary artery shunting to superior vena cava.  
de Mulder M, **Hendriksz TR**, de Jong PL, IJsselmuiden AJ.  
EuroIntervention. 2015 Oct 22;11(6):e1. doi: 10.4244/EIJV1116A132.

Een man met een afwijkende PET-CT-scan.  
**Tamara J. Meulman**, Shiuw H. Ho-Han en **Tadek R. Hendriksz**  
www.ntvg.nl/artikelen

Colorectal liver metastatic disease: efficacy of irreversible electroporation-a single-arm phase II clinical trial (COLDFIRE-2 trial).  
Scheffer HJ, Vroomen LG, Nielsen K, **van Tilborg AA**, Comans EF, van Kuijk C, van der Meijs BB, van den Bergh J, van den Tol PM, Meijerink MR.  
BMC Cancer. 2015 Oct 24;15:772. doi: 10.1186/s12885-015-1736-5.

Irreversible Electroporation for Colorectal Liver Metastases.  
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Schmitz AM, Veldhuis WB, Menke-Pluijmers MBE, Kemp van der WJ, Velden TA van der, **Kock MCJM**, Westenend PJ, Klomp DW, Gilhuijs KG  
Invest Radiol. 2015 Jul 2

### Wetenschappelijke presentaties en posters

7T Breast MRI to Visualize Proliferative Characteristics of Breast Cancer Using DCE, DWI, and 31P-MRS Alexander M. Th. Schmitz<sup>1</sup>, Wouter B. Veldhuis<sup>1</sup>, Marian B.E. Menke-Pluijmers<sup>2</sup>, Wybe J.M. van der Kemp<sup>1</sup>, Tijn A. van der Velden<sup>1</sup>, Marc C.J.M. Kock<sup>3</sup>, Pieter J. Westenend<sup>4</sup>, Dennis W.J. Klomp<sup>1</sup>, Kenneth G.A. Gilhuijs<sup>1</sup> <sup>1</sup> Department of Radiology/Image Sciences Institute, University Medical Center Utrecht, Utrecht, Netherlands; <sup>2</sup> Department of Surgery, Albert Schweitzer Hospital, Dordrecht, Netherlands; <sup>3</sup> Department of Radiology, ISMRM

Radiologendagen, 2015, Rotterdam, 7T Breast MRI, A Schmitz, **M Kock**

Radiologendagen, 2015, Rotterdam. Waarde van X-thorax bij hartfalen. D. Goei, P van der Valk, **M.C.J.M. Kock**

Internistendagen 2015: Sarcopenie bij borstkanker. H. Rier, **M.C.J.M. Kock**, MD. Levin

RSNA 2015, Clinical value of Chest X-Ray in heartfailure. D. Goei, P van der Valk, **M.C.J.M. Kock**

Landelijke studiedag Samenwerking in de Oncologische Zorg, Utrecht. One Stop Shop bij Borstkanker. **M.C.J.M. Kock**, Leids Congres Bureau 14 april

One Stop Shop bij Borstkanker, **M Kock** - Landelijke studiedag Samenwerking in de Oncologische Zorg - Leids Congres Bureau 14 april, Amersfoort

**Promotie: M.C.J.M. Kock, Oponent** bij de verdediging van de thesis van Alexander Schmitz, "Magnetic Resonance Imaging for Therapy Selection in Breast Cancer" UMCU 12 januari 2016.

# Ziekenhuisapothek

## Overige publicaties

Anafylactoïde reactie op acetylcysteïne na een paracetamolintoxicatie: staken of doorbehandelen?

**Schoemakers RJ, Beex-Oosterhuis M, Ponssen HH, Dieleman HG, Tijssen G.**  
PW Wetenschappelijk Platform 2015;9:a1530

## Voordrachten en lezingen

Huisflora

**Veenbaas T.**

PUOZ GMP-z Update - 15 januari 2015

## Posters op geaccrediteerde wetenschappelijke congressen

Is Rapydan® superieur aan Emla® als lokaal anestheticum bij kinderen?

**Erkelens JRS, K.M. Welborn, Beex-Oosterhuis MM**

Wetenschapsdag ASz – 18 juni 2015

Belang en interpretatie hoge clozapinespiegel

**Overbeeke MR, Beex-Oosterhuis MM, Tijssen TAG, Gool van AR**

Wetenschapsdag ASz – 18 juni 2015

# Promoties ASz 2015

In het jaar 2015 hebben zes promoties plaatsgevonden door medewerkers die op moment van promoveren in dienst waren van het ASz, danwel promoties die verricht zijn (mede) op basis van onderzoek in het ASz.

Chirurgie

**Basic research in cardiovascular disease: from stem cells to immunomodulation**

**Lijkwan, M.**

Proefschrift Leids Universitair Medisch Centrum

Chirurgie

**Tailored treatment of metastatic colorectal cancer: clinical and pre-clinical developments.**

**Kuijpers, A.M.J.**

Proefschrift Universiteit van Amsterdam

Leerhuis

**Feedback in Clinical Education**

**Ridder van de, J.M.M.M.**

Proefschrift Universiteit Utrecht

Medische Microbiologie

**Cellular immunotherapy : from stem cell to lymphocyte.**

**Huijskens, M. J.A.J.**

Proefschrift Universiteit Maastricht

Radiologie

**Advances in MRI for colorectal cancer and bowel motility.**

**Paardt van der, M.P.**

Proefschrift Universiteit van Amsterdam

Radiologie

**Prognostic and predictive biomarkers in colorectal cancer, Towards precision medicine**

**Reimers, M.**

Proefschrift Leids Universitair Medisch Centrum

# Verantwoording

De data ten behoeve van het wetenschappelijk jaaroverzicht 2015 zijn verzameld via de leden van de Wetenschapscommissie, de bibliotheek en via de vakgroepen. De bibliotheek heeft actief gezocht in Google Scholar en PubMed. In deel II van het wetenschappelijk jaaroverzicht zijn de PubMed publicaties opgenomen die zijn terug te vinden met de affiliatie Albert Schweitzer ziekenhuis. Dit deel is opgesteld volgens de regels voor biomedische tijdschriften, de Vancouverregels.

Voor deel III, leverden de vakgroepen de overige wetenschappelijke output aan in een vooraf gevraagd format. In dit deel zijn publicaties opgenomen die niet in PubMed zijn terug te vinden en verschenen zijn in tijdschriften die geen impactfactor hebben. In dit deel zijn naast de overige publicaties ook de publicaties in de vorm van een boek of hoofdstuk van een boek opgenomen. Voor 'voordrachten' en 'posters' gold dat deze gepresenteerd zijn op geaccrediteerde wetenschappelijke symposia, congressen nationaal of internationaal.

Voor de genoemde publicaties geldt dat de (co) auteur ten tijde van dataverzameling, data-verwerking of het vastleggen van de resultaten een aanzienlijk deel van de werkzaamheden moet hebben verricht in het Albert Schweitzer ziekenhuis en daar werkzaam moet zijn (geweest). Indien het artikel van de (co) auteur gepubliceerd wordt tijdens de aanstellingsperiode in het Albert Schweitzer ziekenhuis, maar de feitelijke werkzaamheden reeds onder een andere aanstelling zijn verricht, kunnen de artikelen niet in het Wetenschappelijk Jaaroverzicht van het Albert Schweitzer ziekenhuis worden opgenomen. De digitale publicaties voorafgaand aan de geprinte versie (Epub ahead of print) van 2015 zijn zoveel als mogelijk meegenomen in het jaaroverzicht als ze nog niet op papier zijn verschenen.

# Colofon

Dit wetenschappelijk jaaroverzicht van het Albert Schweitzer ziekenhuis wordt uitgegeven door het Leerhuis. De redactie is Rianne van Hof en Moniek Kuipers-Freijssen van de bibliotheek zeer erkentelijk voor het verzamelen van de Pubmed en overige publicaties en het corrigeren van het rapport daar waar nodig.

**Uitgave:** Wetenschappelijk jaaroverzicht 2015

## **Redactie**

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## **Vormgeving**

Elan Strategie en Creatie, Rijswijk

## **Productie en contact**

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**Oplage:** digitaal

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