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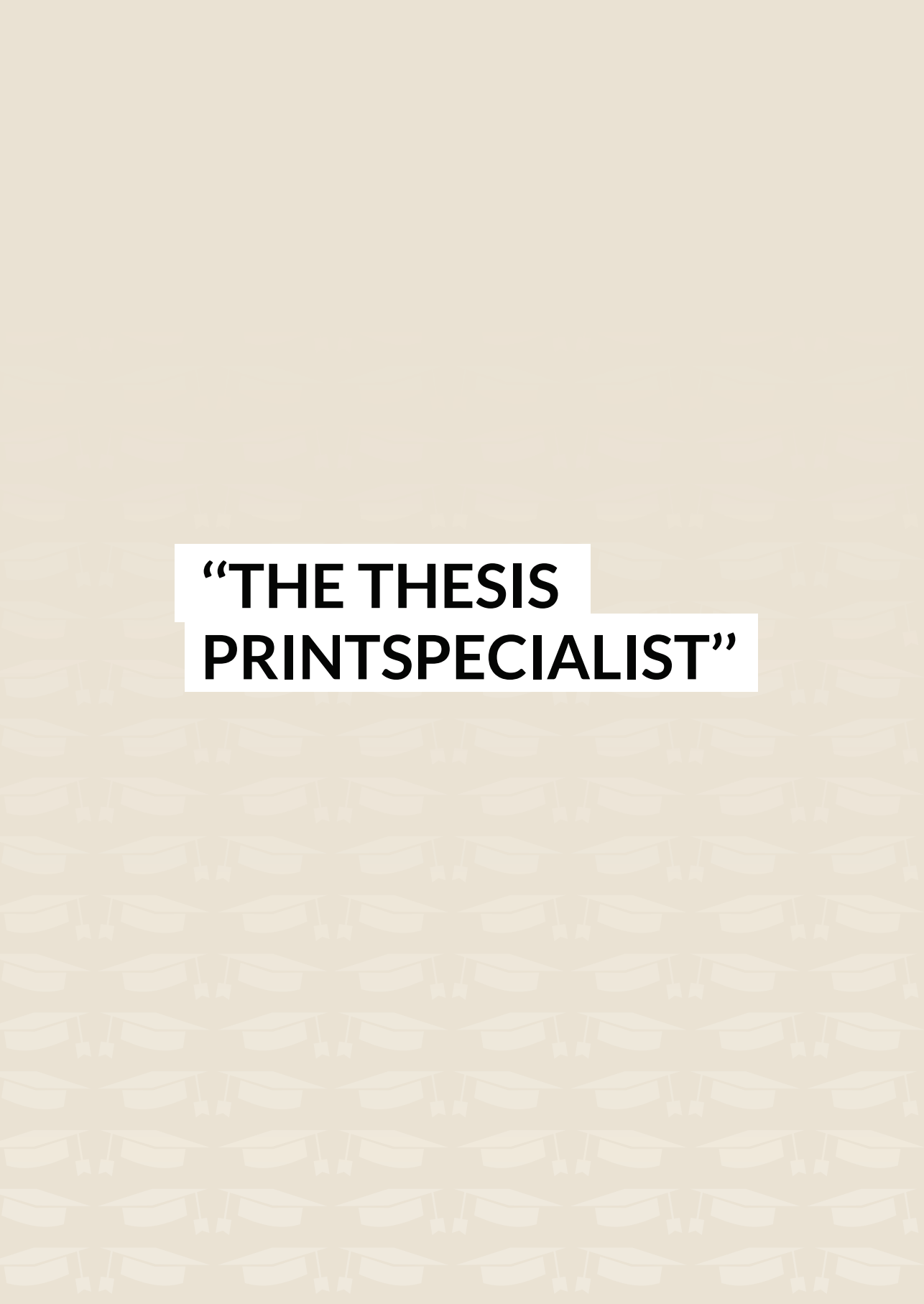
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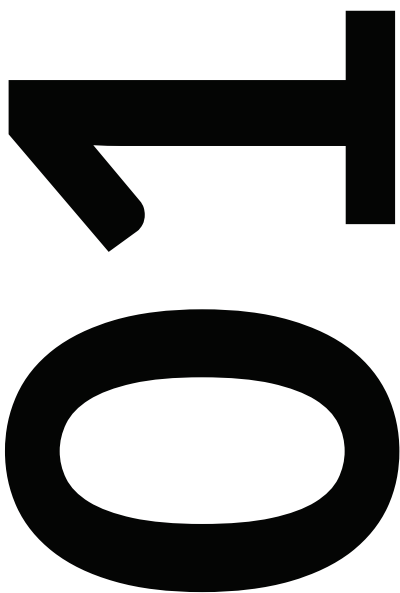
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METHOD AND DELIVERY TIMES

METHOD
DELIVERY TIMES
SUITABLE OFFER
DELIVERY OF FILES
OUR LAYOUT/DESIGN OF THE THESIS/BOOK
INTERIOR AND COVER
ISBN
THE TEST PRINT
CORRECTION ROUNDS
PAYMENT
FINAL PRINTING AND BINDING
SENDING

METHOD & DELIVERY TIMES

Method

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We can assist you in several phases of the process. You can let us take care of formatting your thesis, but it is of course also possible that you want to do the formatting yourself. Below you find an overview of the process that we normally use and the associated delivery schedule.

- Suitable offer
- Delivery of Files
- Making a test print
- Layout interior and the cover provided by us
- Producing a test print
- Correction rounds
- Payment
- Final printing and binding
- Sending

In case you want us to design the layout of the interior and the cover, we will do so after you have accepted our offer and provided us with the necessary files.

Delivery times

Layout inside: 10 working days

Printing and binding: 5 working days

If possible, we encourage you to make more time available, so that the process can be executed in a calm and careful manner.

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The offer consists of an overall price (excluding 6% VAT) for the entire production process of your thesis at the highest quality, including a bookmark / invitations , statements in black and white, a test print (bound and sent by mail), adjustments during required correction rounds and delivery to an address in the Netherlands.

The amount in the offer is always exclusive of VAT. For theses a VAT rate of 6 % applies.

Do you agree with the offer we have made for you? Please let us know by phone or email.

Delivery of files

You can deliver the files in different ways to us. Below are two options for delivery.

- On USB-stick
- By wetransfer.com

We prefer not to receive the files by email because it usually involves large files. Through e-mail we are always accessible for questions or comments.

Our design of the thesis interior and cover

If you want us to take care of the layout of the interior and / or cover?, we are pleased to do so.

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On average we need 10 working days to format your thesis.

Formatting the cover is included in our services, free of additional charge.

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Test Print

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ISBN

By giving your thesis an ISBN (International Standard Book Number) bookstores and libraries are able to find your thesis.

We can provide the ISBN application for you.

For this, we need the following information:

- First and last name
- Title thesis
- Subtitle thesis
- Discipline (for the purpose of a NUR-number)
- Number of pages

The test print

We will make a test print for you on the selected paper. The test print will be bound, so you will get a clear view of what the result will look like.

We will send you the test print so you can check it and comment on it. Of course it is always possible to meet with us in case you have specific questions.

Correction Rounds

After you reviewed the test print you can indicate any changes that should be made in the test print (pdf) itself. We will ensure that these points are adjusted. We consider it important that the end result is completely to your liking, regardless of how many correction rounds may be needed for this. That is why we do not work with a fixed number of correction rounds. Once you approve of the last send pdf we would like to receive a confirmation thereof by e-mail.

Payment

Before we proceed to the final printing you will receive an invoice from us. The invoice amount should be transferred to our bank account on the day you will pick up the thesis booklets/books/prints or the day that we will send your thesis.

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Final printing and binding

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On page 32 you will find more information about the different types of paper that are available

for both the interior as well as for the cover. You can already choose these at the beginning of the process so that the test print already will be printed on the right paper.

First, the covers will be printed, after which they will be laminated and cut to the correct size. Then the interior will be printed, and if this is also cut to the correct, the binding will take place.

We digitally print in the highest possible quality and on class A paper (FSC certified). We ensure that your thesis will remain well-bound by our specially developed way of binding through a combination of “Hotmelts”.

Sending

We send your thesis by courier for free to an address in the Netherlands. This will take about one day, please take this into account in your planning.

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COVER

COVER OPTIONS

EXAMPLES COVERS

COVER

We would like to design your cover free of charge for you or help you with this. This is included in our service. This also applies to the bookmark.

On our website Proefschriftenprinten.nl you will find information about the designs of a cover, if you want to take care of the design yourself.

Cover options

Hard cover

It is possible to order some hard cover versions of your thesis. Please inform us if you wish to receive such versions/copies so that we can take care of the additional printings with hard covers.

Laminating

Laminating is the application of a plastic layer on the cover, used to preserve the quality of the prints of your thesis. You can choose between glossy and matte laminate.

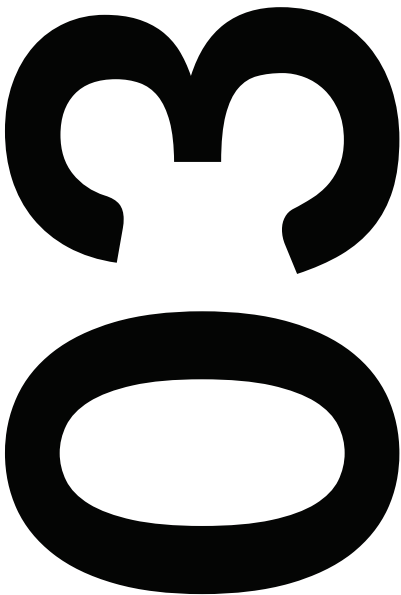
Spot UV varnish

Spot UV varnish is a glossy layer applied to specific areas on the cover. It is only suitable for matt laminated covers.

Cover with invitation

Paper size: SRA3 45 x 32 cm





LAYOUT INSIDE

TIPS FOR SELF-DESIGNING THE INSIDE
PAGES IN WORD!

RESIZE

DESIGN THESIS

TIPS ABOUT FORMATTING IN WORD.

LAY-OUT INSIDE

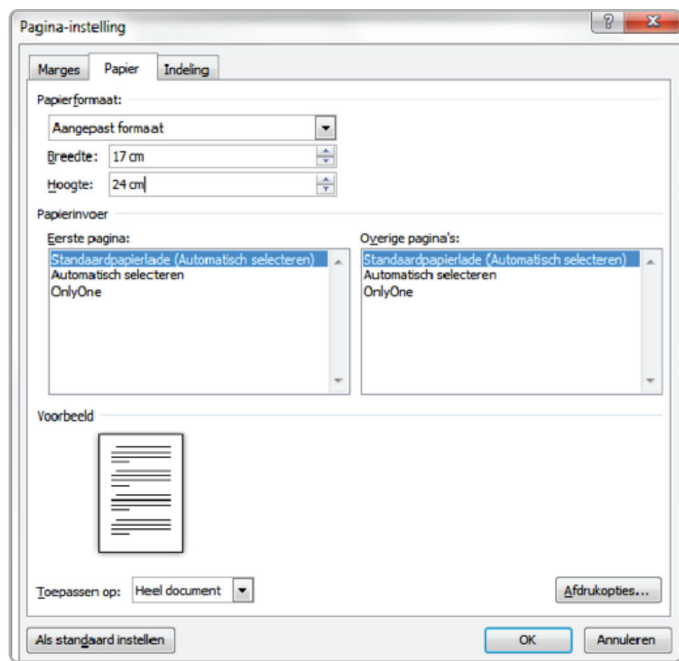
Here you will find information regarding the preparation of the interior of your thesis. We have tried to provide you with extensive information, so you will not encounter problems with designing the layout of your thesis. If you still have questions please contact us so we can discuss this together. Good luck with the layout!

Tips for self-designing the inside pages in Word!

You can format your thesis in different styles. The standard format of a final thesis is 17 x 24 cm. When you your files in A4 format we will reduce the file to 81 %, so the final size will still be 17 x 24 cm (of course without text jumps).

Resize

By default, the Page Setup is to A4. If you want to change this into 17 x 24 cm, proceed as follows:



Page layout, format, more paper sizes, custom sizes, and you can set the width and height, set on 17 and 24 cm. When you format your thesis to 17 x 24 cm, we recommend the following:

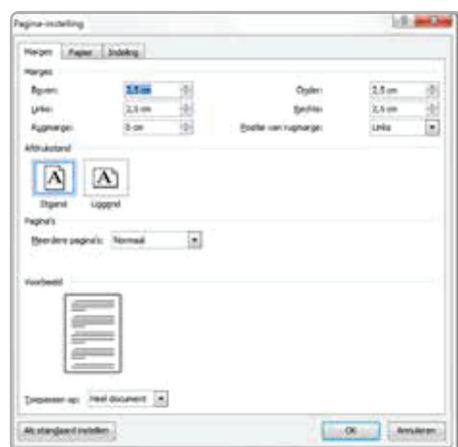
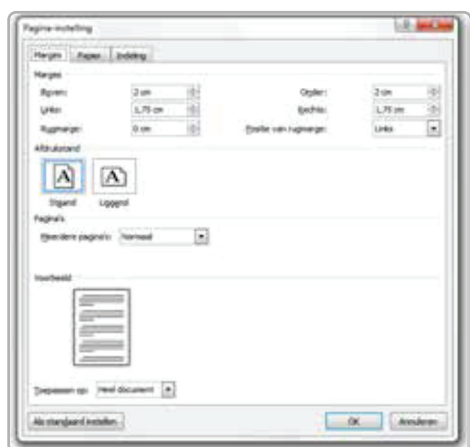
- Keep a font size of 9.5
- Hold all margins on 2,5 cm

When you format your thesis to A4 size, we recommend the following:

- Hold a letter-to large to 12 cm
- Hold all margins at 2.5 cm

We advise you to choose an easy and readable font.. A commonly used font is Myriad Pro, but this is purely a matter of taste! The default line spacing that is used is 1.2 - 1.4, this ensures that the text remains readable. We can advise you if you want.

For printing images in a nice and sharp result, you need 300 DPI as a minimum resolution. When using graphs, we recommend using the highest possible resolutions. In addition, use a minimum line width of 0.5. As the thesis is printed digitally, you do not have to restrict colored figures or graphs to fixed sections of your thesis so that any colored pages can be randomly scattered



throughout the thesis.

If you get stuck and / or like to get advice in the preparation of your thesis, you can always contact us!

100% Quality: with modern printers today there is no difference observed between press and print

Design thesis



300 DPI



72 DPI

We advise you to follow the information from the university about design and text used in the doctorate regulations.

We like to give you a possible example.

- **First page: (French) title page**, this only contains the title and possibly the name of the author
- **Second page: Colophon**, The following information may be included here:
 - ISBN number
 - Mentioning Print Service Ede in one of the following possibilities:
 - Printed by: Print Service Ede
 - Printed by: Print Service Ede - Ede
 - Printed by: Print Service Ede - www.proefschriftenprinten.nl
 - Printed by: Print Service Ede - The Netherlands
 - Copyright
 - Sponsors
- **Third page: Promotion pages**, here is all the information that your university prescribes about the promotion committee
- **Fourth page: Promotion Committee**, here comes the listing of all members of the Promotion committee
- Preface
- Table of contents
- Introduction
- Chapters
- Appendix
- Summary
- Production list
- Curriculum Vitae

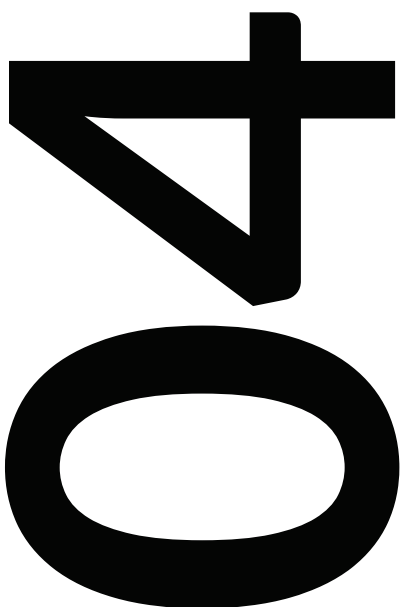
Tips about formatting in Word.

We advise you to first take note of the possibilities provided in WORD format.

You can easily use headings and subheadings. Bookmarks can be created for an automatic table of contents. You can specify that you want to start on a new page at the end of the previous chapter. You can also create sections after each chapter to add page numbers and titles in the header of your dissertation.

Would you like us to take of this creation, we can help you off course.

Very important is the text check on spelling, grammar and punctuation. Early correction prevents a lot of waste of time afterwards. Off course you are fully responsible for the content and correct text.



LAY-OUT

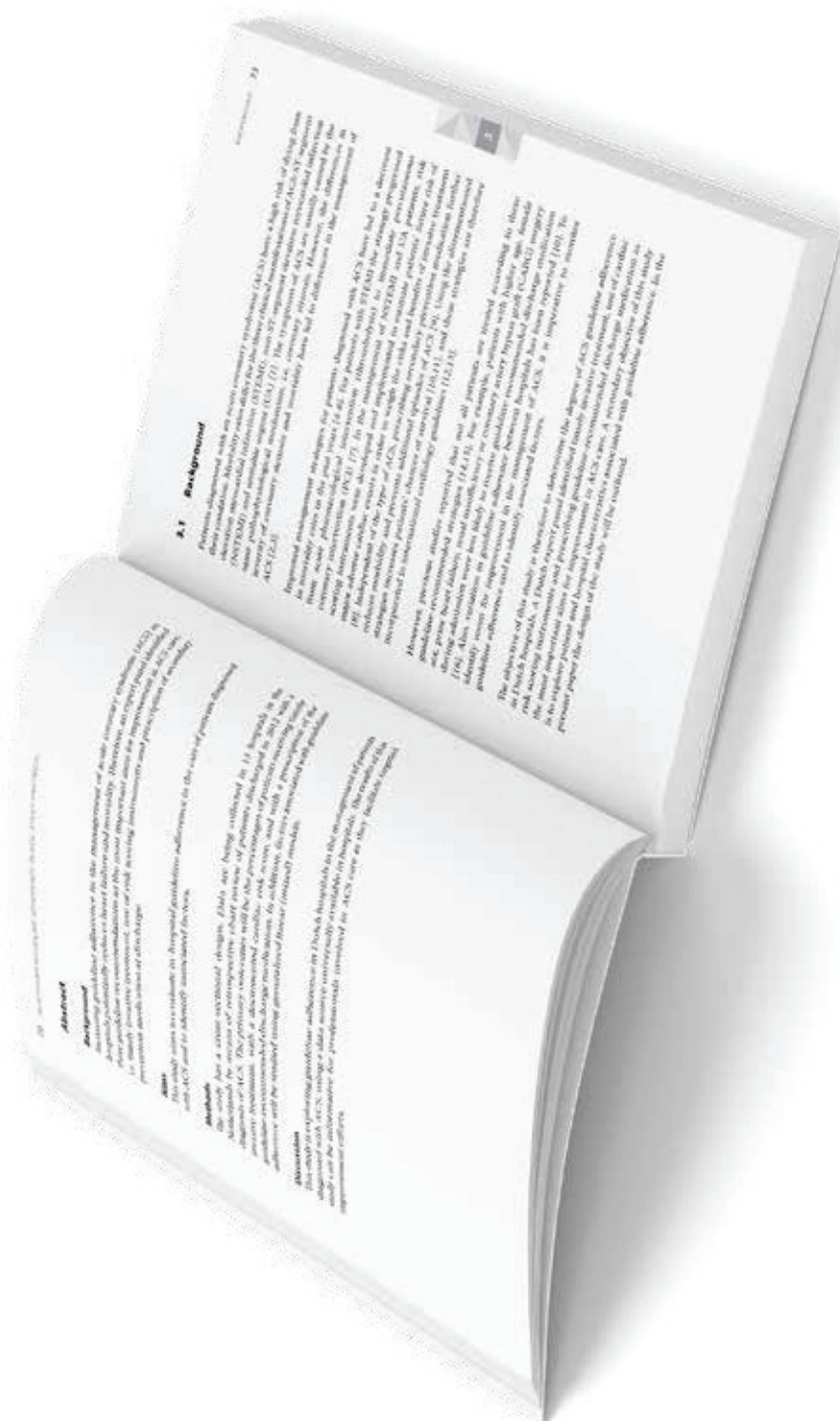
EXAMPLES

Example lay-out cover & bookmark



Example lay-out inside + interleaves





50

TYPES OF PAPER

LAMINATING

100 GSM G-PRINT

90 GSM HVO

90 GSM BIOTOP

TYPES OF PAPER

At Proefschriftenprinten.nl you can choose from different types of paper for inside pages as well as for the cover. All paper we use is FSC certified.

For the interior, we can choose from the following paper:

- G-print 100 gsm *
- Biotope 90 gsm (cream)
- HVO (wood free offset) 90 gsm

* This paper we use most often for printing the inside pages.

For the cover, we have a choice of the following paper:

- Ensocoated 250 gsm**
- Majestic 250 gsm

**This paper, we use the most for printing covers.

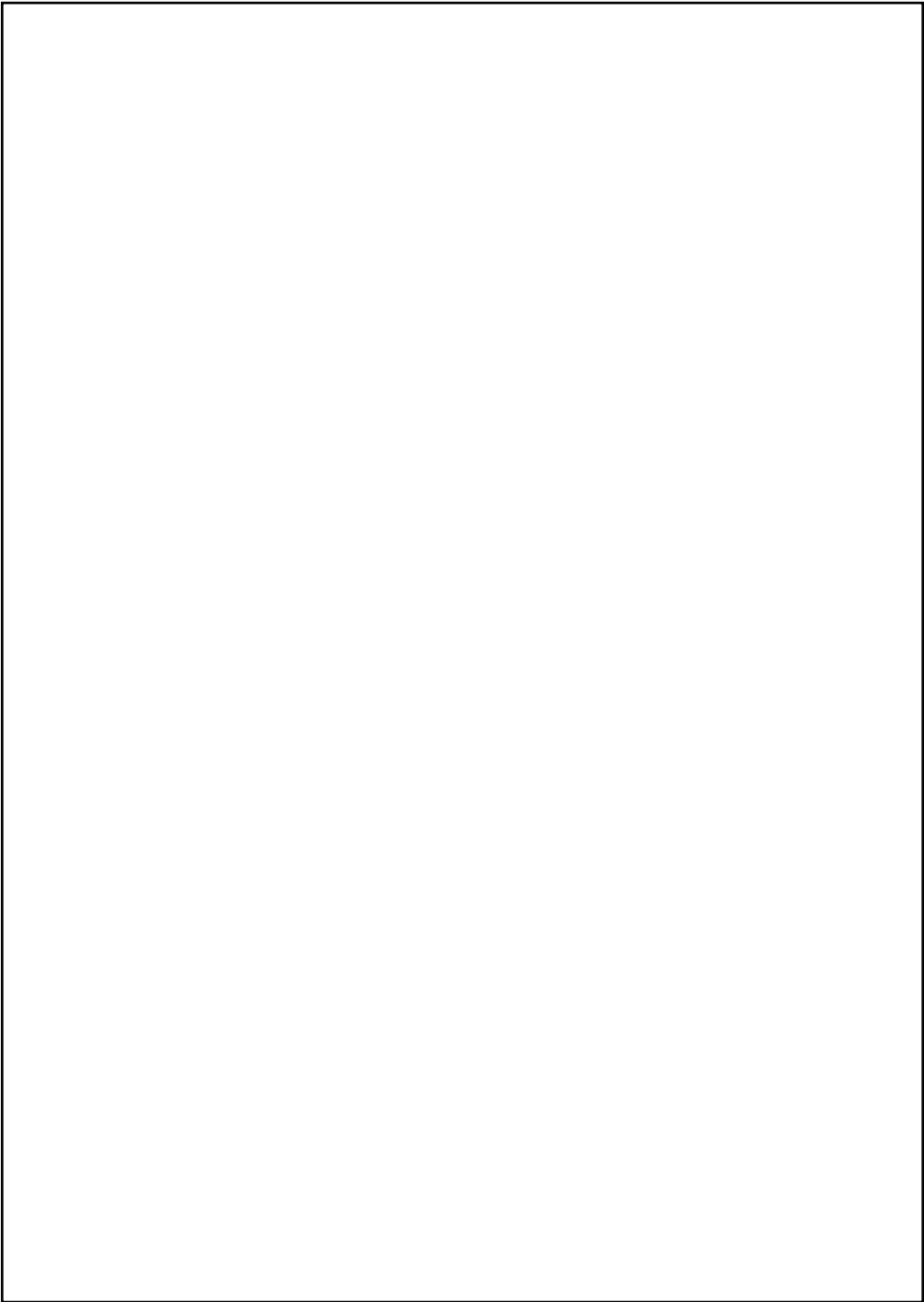
We can send you a sample of the different types of paper, but you are of course welcome to visit us and consult our employees.

Laminating

We always laminate the covers to improve the preservation of the thesis: the cover is robust, more resistant to damage, and remains in a good condition. You can choose between gloss and matt lamination. The quality and prices are exactly the same.

Besides gloss or matt you can also choose a spot UV, this is a shiny layer over a part of the cover, so that a certain extra element particularly draws attention.

100 GSM G-PRINT



CHAPTER 3

Content validity and psychometric characteristics of the “Knowledge about Older Patients Quiz” for Nurses using Item Response Theory

Dikken J

Hoogerduijn JG

Kruitwagen CLJJ

Schuurmans MJ

*Journal of the American Geriatrics Society 2016;
(64)11:2378-83*

CHAPTER 3

Abstract

Objectives: To assess the content validity and psychometric characteristics of the Knowledge about Older Patients Quiz (KOP-Q), which measures nurses' knowledge regarding older hospitalized adults and their certainty regarding this knowledge.

Design: Cross-sectional.

Setting: Content validity: general hospitals. Psychometric characteristics: nursing school and general hospitals in the Netherlands.

Participants: Content validity: 12 nurse specialists in geriatrics. Psychometric characteristics: 107 first-year and 78 final-year bachelor of nursing students, 148 registered nurses, and 20 nurse specialists in geriatrics.

Measurements: Content validity: The nurse specialists rated each item of the initial KOP-Q (52 items) on relevance. Ratings were used to calculate Item-Content Validity Index (I-CVI) and average Scale-Content validity Index (S-CVI/ave) scores. Items with insufficient content validity were removed. Psychometric characteristics: Ratings of students, nurses, and nurse specialists were used to test for different item functioning (DIF) and unidimensionality before item characteristics (discrimination and difficulty) were examined using Item Response Theory. Finally, norm references were calculated and nomological validity was assessed.

Results: Content validity: Forty-three items remained after assessing content validity (S-CVI/ave = 0.90). Psychometric characteristics: Of the 43 items, two demonstrating ceiling effects and 11 distorting ability estimates (DIF) were subsequently excluded. Item characteristics were assessed for the remaining 30 items, all of which demonstrated good discrimination and difficulty parameters. Knowledge was positively correlated with certainty about this knowledge.

Conclusion: The final 30-item KOP-Q is a valid, psychometrically sound, comprehensive instrument that can be used to assess the knowledge of nursing students, hospital nurses, and nurse specialists in geriatrics regarding older hospitalized adults. It can identify knowledge and certainty deficits for research purposes or serve as a tool in educational or quality improvement programs.

Keywords

KOP-Q; Knowledge; Certainty; Nurses; Older adults; Item response theory

VALIDATION OF THE KNOWLEDGE ABOUT OLDER PATIENTS - QUIZ

Introduction

As a result of demographic changes, nursing care in hospitals increasingly involves older adults.^{1,2} Several studies suggest that nurses' negative attitudes toward and limited interest in older adults affects quality of care.³⁻⁵ Because increasing nurses' knowledge of geriatrics might positively influence attitudes,⁶ measuring nurses' knowledge is the first step toward change.

Although a number of instruments that measure the knowledge of hospital nurses regarding older adults are available, they are considered outdated or too country specific; they mix the measurement of knowledge with measurement of opinions, beliefs, and experiences; or they lack inclusion of care perspectives.^{3,4,7} Furthermore, the absence of a clearly described content development often limits their validity. To address these concerns, a new measurement instrument was developed: the Knowledge about Older Patients Quiz (KOP-Q). The content and development processes have been described, and initial validity studies demonstrated promising results.⁷ The KOP-Q (in Dutch) contains 52 dichotomous items (true/false) measuring general knowledge regarding older hospitalized adults. Each item is combined with a certainty scale that allows respondent to indicate their level of certainty regarding the answer given (0–100% certainty). This rating is helpful in increasing awareness of one's personal knowledge level.

The studies described in this article assess the content validity and psychometric characteristics of the KOP-Q.

3

CHAPTER 3

Method

Two studies were conducted, each using a cross-sectional design. The medical review board of the University Medical Center Utrecht reviewed and approved the studies (METC protocol numbers: 12–302/C and 14–345/C). All participants provided informed consent.

Study 1: Content validation*Participants and Measurement*

Content validity was assessed using a previously developed method.^{8,9} Dutch nurse specialists ($n = 60$) with a master's degree in geriatric or gerontological nursing or a doctorate in nursing or a related field were contacted through their formal network. Nurse specialists who were willing to participate received an e-mail invitation to rate the relevance of the KOP-Q items regarding construct, study population, and purpose on a 4-point Likert scale (highly relevant = 4, quite relevant = 3, somewhat relevant = 2, not relevant = 1). Comprehensiveness was measured by asking the nurse specialists whether the items covered the entire construct measured.

Statistical Analysis

The Item Content Validity Index (I-CVI), defined as the proportion of experts who rate the content as valid (relevance rating of 3 or 4), was calculated for each item.^{8,9} Items were rated excellent when the I-CVI value was greater than 0.78. The Fleiss kappa statistic (k^*), an index of agreement among experts regarding the relevance of an item, was calculated to correct for chance agreement. Items considered excellent ($k \geq 0.74$, I-CVI ≥ 0.78)^{10,11} were retained for Study 2. Items on the threshold ($k = 0.74$, I-CVI = 0.75, having 12 raters) were individually assessed. For complete scale validation, all I-CVI values were averaged to calculate a Scale Content Validity Index (S-CVIave), for which a value greater than 0.90 is considered excellent.⁹ Data were analyzed using SPSS version 22.0 (IBM Corp., Armonk, NY).

Study 2: Psychometric characteristics, norm references, and nomological validity*Participants and Measurement*

Psychometric testing of the KOP-Q was conducted using the KOP-Q ratings of first- and final (fourth)-year bachelor of nursing students, hospital registered nurses (AD or BSN), and nurse specialists (MSc) in geriatrics to ensure a wide range of knowledge ability and to conduct known group validation. All of the nursing students were recruited at one university of applied sciences. Students were asked to participate by e-mail and to complete the KOP-Q online. Over a 3-month period, registered nurses working with older adults on different wards were recruited from two general hospitals. Nurses received an e-mail from their ward manager inviting them to participate and asking them to complete the KOP-Q online. Nurse specialists attending a formal nurse specialist in geriatrics network meeting were requested to complete a paper-and-pencil version of the KOP-Q. None of the participants in Study 2 participated in Study 1.

VALIDATION OF THE KNOWLEDGE ABOUT OLDER PATIENTS - QUIZ

Statistical Analysis*Step 1: Unidimensionality and Psychometric Characteristics*

First, missing values were assessed to determine whether list-wise deletion could be used. Second, unidimensionality, which is a critical assumption for Item Response Theory (IRT), was assessed. Items were first tested regarding the demonstration of uniform differential item functioning (DIF) using the transformed item difficulties (TID) method.¹² An item is said to function differently (to be a DIF item) when individuals from different groups have different probability distributions of answering an item correctly despite having the same knowledge level.¹³ For example, a first-year student having the same knowledge level as a fourth-year student should have the same probability distribution of answering an item correctly, if not, the item presents DIF. DIF suggests that the item is measuring an additional construct or dimension that may or may not be relevant to the intended construct and that it, therefore, violates the unidimensional assumption.¹² The default value or cutoff score for classifying items as DIF was set at 1.5, which is a commonly used value.¹⁴⁻¹⁷ All items demonstrating DIF were extensively discussed until consensus was reached among two nurse specialists and two researchers, validating DIF item removal. Modified parallel analysis (MPA) was then used to examine the (uni)dimensionality of remaining items;^{17,18} this analysis tests whether the explained variance of the dimensions is significantly higher than expected. For the unidimensionality assumption to hold, the p-value for the second factor (or higher) must be nonsignificant.^{17,18}

Third, several parameters can be assessed in IRT. The alpha parameter (α) is the discrimination factor, and high α values indicate that the item is better at discriminating between knowledgeable and less-knowledgeable respondents. The beta parameter (β) corresponds to the knowledge level at which the probability of answering correctly is the same as answering incorrectly; it is also called the difficulty parameter. The c parameter (c) represents a guessing factor and describes the probability that a respondent with no knowledge will answer the item correctly.¹⁹ Before the parameters can be estimated, it is important to assess the fit of the data to the model. A Rasch model, which postulates a one-parameter model (only the alpha parameter is present), was tested against a two-parameter model (PL2, containing the alpha and beta parameters). Next, the two-parameter model was tested against a three-parameter model (PL3, containing the alpha, beta, and c parameters). These different models were compared by applying a deviance test (likelihood-ratio test) and comparing the differences in the Akaike information criterion (AIC). The AIC uses a penalty term for the number of estimated parameters in different models to prevent the model from overfitting a statistical problem that occurs when the fitted model describes noise instead of the true structure of the data; lower AIC values indicate a better fitting model.²⁰

Step 2: Norm References

In IRT, the estimates of discrimination and difficulty parameters are analyzed at the

3

5

Types of paper

CHAPTER 3

individual level,¹⁹ but for practical use, classical test theory (CTT) is more appropriate. In CTT, a test scores is simply the sum of correctly answered items. These summed scores are then compared with the test scores generated through IRT analysis using a Pearson correlation test. The CTT approach can be used if the CTT scores are close to the scores of the IRT-derived tests. First, a normal distribution of CTT test scores was assessed. Then, norm references (group level), threshold scores, and adjusted Cohen d effect sizes were calculated. Cohen d was used to estimate the (standardized) differences between groups.

Step 3: Nomological Validity

Unidimensionality of the KOP-Q construct “certainty” was tested using confirmatory factor analysis. The fit of the model was assessed using the comparative fit index (CFI) and the root mean square error of approximation (RMSEA). Values greater than 0.90 for CFI and less than 0.06 for RMSEA were considered to indicate acceptable model fit.²¹ The hypothesis that higher knowledge scores would be positively correlated with higher certainty (reflection) scores was tested using a Pearson correlation test. Ltm, an R package for latent variable modeling and item response theory,¹⁷ was used to assess the dimensionality of knowledge and certainty items and to perform the model fit and IRT analysis. SPSS version 22.0 was used to test the correlation between IRT test scores and CTT test score; to calculate norm scores, threshold scores, and adjusted Cohen d effect sizes using CTT test scores; and to assess the nomological validity of the knowledge construct.

Results

Study 1: Content Validity

Of the 60 nurse specialists invited, 12 (20.0%) agreed to participate. Respondents were primarily female ($n = 9$) and had a mean age of 52.0 ± 5.7 , a mean 25.0 ± 9.8 years of experience in nursing, and an average 7.6 ± 4.6 years of experience in their current area of practice geriatric nursing ($n = 9$) or teacher in geriatrics at the bachelor level ($n = 2$); data on experience were missing for one nurse specialist. Nine items were excluded from the initial KOP-Q after assessment of content validity (Appendix S1). The S-CVlave was 0.91 (range 0.75–1.00). Items of the KOP-Q were considered comprehensive, and no suggestions for extension were made.

Study 2: Psychometric Characteristics, Norm References, and Nomological Validity

Of the invited participants, 130 first-year students (69.1%), 90 fourth-year students (57.7%), 179 registered nurses (50.0%), and 21 nurse specialists (35%) agreed to participate. In the participating sample, list-wise deletion was used when nonresponse occurred; this was the case for 12 first-year students (9.2%), nine fourth-year students (10%), and seven registered nurses (3.9%) and when respondents had missing values in the KOP-Q items (11 first-year

VALIDATION OF THE KNOWLEDGE ABOUT OLDER PATIENTS - QUIZ

students (8.5%), 3 fourth-year students (3.3%), 24 registered nurses (13.5%), one nurse specialist (4.8%). The sociodemographic characteristics of respondents with missing values were not significantly different from those with complete data (all $P > .05$). Sociodemographic characteristics for the 353 respondents with no missing data on the KOP-Q are presented in Table 1.

Table 1. Characteristics of participants with no missing Knowledge about Older patients-Quiz values (n=353)

Characteristic	Nursing Students, First Year, n = 107	Nursing Students, Final Year, n = 78	Registered Nurses, n = 148	Nurse Specialists, n = 20
Female, %	89.6	90.7	88.5	95.0
Age, mean±SD	18.6 (1.8)	22.5 (2.5)	34.7 (11.0)	45.6 (8.8)
Hours per week working as a nurse, mean±SD	-	-	29.2 (7.0) ^a	31.9 (4.6) ^b
Highest qualification, n (%)	-	-		
Associate degree			59 (39.9)	1 (5.0)
Bachelor of science in nursing			59 (39.9)	2 (10.0)
Post-bachelor of science in nursing			25 (16.9)	-
Master of science in geriatric or gerontological nursing			4 (2.7)	15 (75.0)
Doctorate in nursing or related field			-	2 (10.0)
Other			1 (0.6)	
Type of ward where currently working, n (%)	-	-		
Critical care unit			12 (8.1)	
Orthopedics			6 (4.1)	1 (5.0)
Internal medicine			26 (17.6)	
Geriatric medicine			7 (4.7)	17 (85.0)
Cardiology			12 (8.1)	
Neurology			14 (9.5)	
Lung diseases			19 (12.8)	
Gastrointestinal, liver			38 (25.7)	
Surgical			13 (8.8)	
Education				1 (5.0)
Missing			1 (0.6)	1 (5.0)

Missing: n=3, ^b2. SD= standard deviation.

CHAPTER 3

Step 1: Unidimensionality and Psychometric Characteristics

Of the 43 KOP-Q items resulting from Study 1, 12 demonstrated distorted ability estimates (DIF score >1.5), suggesting that the item was measuring an additional construct or dimension. Eleven of these were excluded. The DIF item “For older people, bed rest is important to enhance recovery” was considered too important to exclude because the content of no other item in the KOP-Q covered this question. Two additional items demonstrated ceiling effects and were excluded. As a result, 13 items (7, 9, 17, 21, 23, 26, 28, 30, 40, 41, 43, 44, 51) were excluded from the KOP-Q (Appendix S1), leaving 30 items for further analysis. The MPA test of unidimensionality for the 30 KOP-Q items was not significant ($P = .29$), which supports the assumption of unidimensionality.

Finally, the best-fitting model for the data was assessed. The 2PL model demonstrated a significantly better fit ($P < .001$) than the 1PL model. The 3PL model demonstrated no significantly better fit than the 2PL model ($P = .66$) and had a higher AIC, so the 2PL model (estimating discrimination and difficulty parameters) was considered the best fit. Table 2 presents the discrimination parameter (α) and difficulty parameter (β) estimates of the resulting 30 items of the KOP-Q. Most items had moderate to high discrimination values. The range at which the KOP-Q retrieves information about the knowledge level of participants is a β of -10.2 to 0.7 , indicating that most items are easy to answer even if knowledge levels are low. The reliability of the final set of knowledge items was good (Kuder-Richardson formula 20 = 0.70).

Table 2: Item characteristics of the 30-item true-false Knowledge about Older Patient-Quiz

Item	Short item description (originally written in Dutch)	Discrimination parameter	Difficulty parameter
1	Forgetfulness, concentration problems, and indecisiveness are parts of aging rather than indicators of depression.	0.812	0.037
4	For older people, bed rest is important to enhance recovery.	1.396	-1.579
5	Individuals with a cognitive disorder, such as dementia, are at greater risk for delirium.	0.754	-3.026
6	In general, older people are more sensitive to medication because their kidney and liver functions are declining.	0.787	-1.806
8	People rarely remember that they were anxious or restless during delirium.	0.932	-0.070
10	In the case of delirium, bright lighting should always be used to illuminate all of the corners of the room.	0.369	-3.254
11	In the case of delirium, activities should be spread out evenly over the day.	0.677	-4.590
12	Depression is recognized in older people less frequently than it is in younger people.	1.593	-1.828
13	In the case of depression, memory problems may occur.	0.473	-5.711

VALIDATION OF THE KNOWLEDGE ABOUT OLDER PATIENTS - QUIZ

Table 2: (continued)

Item	Short item description (originally written in Dutch)	Discrimination parameter	Difficulty parameter
19	It is good to provide extensive instruction about how to complete tasks to individuals with apraxia.	1.038	0.713
20	Pressure that cuts off the blood supply to tissue for two hours may result in pressure ulcers.	0.287	-7.424
22	Identify pressure ulcers only if blister formation or abrasions have occurred.	0.722	-3.134
24	Stress incontinence may occur in people who are not capable of opening their own trousers.	0.227	-2.276
25	Unexpected urinary incontinence in an older person may indicate that the person has a urinary tract infection.	1.040	-2.002
27	Incontinent individuals must have their soiled clothing changed but do not need to be placed on the toilet afterward.	0.843	-3.609
29	Malnutrition can have negative effects on thinking and observation skills.	0.374	-10.207
31	An older person with a body mass index greater than 25 kg/m ² cannot be undernourished.	1.156	-2.029
32	Older people need less fluid because they exercise less.	0.855	-3.839
33	It is good to have older people drink more often because they have a reduced thirst sensation.	0.423	-5.846
35	Lowering the frequency of a medication is an effective intervention to achieve (medication) adherence by patients.	0.949	-1.125
36	Medication may cause geriatric problems such as memory deficits, incontinence, falling, and depression.	0.985	-1.933
37	In the case of difficulty swallowing, all medicines must be ground to ensure that patients ingest them.	1.042	-0.297
38	Pain medication should be administered to older people as little as possible because of the possibility of addiction.	0.717	-2.769
39	Risk of falling is higher for people in the hospital setting than those living at home.	1.155	0.624
42	Asking an individual whether he or she has fallen in the past 6 months is a good way of assessing for risk of falling.	0.934	-2.274
45	Meeting with families during patient assessment is required only for persons with dementia.	1.020	-2.590
46	Overburdening of family caregivers may lead to abuse of the person for whom they are providing care.	1.614	-1.728
49	Most family caregivers do not need additional support from homecare services.	0.632	-3.612
50	As a nurse, you have to speak clearly into the ear of a hearing-impaired older adult.	0.419	-0.301
52	When speaking to hearing-impaired older adults, it is best to speak at normal volume.	0.586	0.476

The item numbers shown correspond to those in online Appendix 1.

90 GSM HVO





**TRANSIENT VON
WILLEBRAND
FACTOR-MEDIATED
PLATELET INFLUX
STIMULATES LIVER
REGENERATION
AFTER PARTIAL
HEPATECTOMY IN
MICE**

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CHAPTER 4

Abstract

Background & aims: In addition to their function in thrombosis and hemostasis, platelets play an important role in the stimulation of liver regeneration. It has been suggested that platelets deliver mitogenic cargo to the regenerating liver, and accumulation of platelets in the regenerating liver has been demonstrated. We studied kinetics of platelet influx in the regenerating liver and investigated the signal that initiates platelet influx.

Methods: We visualized platelets in the liver remnant after partial hepatectomy in mice using intravital microscopy and assessed liver regeneration by examination of liver/body weight ratio and the number of proliferating hepatocytes examined by immunohistochemistry.

Results: We demonstrated rapid but transient platelet influx into the liver remnant after a partial liver resection. Liver regeneration in thrombocytopenic mice was substantially impaired as evidenced by a reduced liver-to-body weight ratio and decreased numbers of proliferating hepatocytes at day 3 compared to mice with normal platelet counts. In contrast, liver regeneration was only mildly impaired when thrombocytopenia was induced 2 hours after partial liver resection. Platelet influx into the liver remnant was virtually absent in the presence of an antibody to von Willebrand factor (VWF) suggesting that VWF release from liver sinusoidal endothelial cells mediates platelet influx. Additionally, liver regeneration in mice deficient in VWF was markedly impaired.

Conclusions: A rapid but transient VWF-dependent platelet influx into the liver remnant drives platelet-mediated liver regeneration.

TRANSIENT VON WILLEBRAND FACTOR-MEDIATED PLATELET INFLUX STIMULATES LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN MICE

Introduction

The liver has a unique regenerative capacity following damage or surgical resection. Liver regeneration starts with a well-organized and complex series of signals which is generated by cytokines and growth factors (1). Accumulating evidence from *in vitro* and *in vivo* studies suggests that platelets have a pivotal role in liver regeneration (2-11). In animal models in which platelets were depleted or functionally impaired, liver regeneration was substantially delayed after a partial liver resection (2,3). Conversely, induction of thrombocytosis stimulated liver regeneration (3,4,12). In a clinical study, we showed that a decreased platelet count is an independent predictor of delayed postoperative liver function recovery after a partial liver resection (10). More recently, it was demonstrated that intraoperative platelet count and platelet transfusion were associated with faster liver regeneration in living donor transplant recipients (11). The molecular mechanisms of platelet-mediated stimulation of liver regeneration are, however, still largely unknown (13).

Platelets bind to liver sinusoidal endothelial cells *in vitro* and this interaction stimulates hepatocyte proliferation (14). In addition, platelets were found to accumulate in the liver parenchyma after a partial liver resection in experimental animal models (3,9). A direct interaction between platelets and hepatocytes is crucial for platelet-mediated stimulation of hepatocyte proliferation *in vitro* (5) but the significance of these findings for liver regeneration *in vivo* are unclear (15). Release of growth factors that are stored within platelets may be responsible for platelet-mediated liver regeneration (5,16,17), but direct evidence from *in vivo* experiments for this is lacking (15,18). For example, release of serotonin from platelet dense granules has been suggested by some to mediate platelet-mediated liver regeneration in mice and humans (2,16). However, although mice lacking serotonin in their platelets have reduced regenerative capacity, this may be explained by a reduced functional capacity of serotonin-deficient platelets rather than by a specific defect in mitogenic activity of the platelets (19). Furthermore, human studies have provided additional evidence against a role of serotonin in liver regeneration in humans (20).

An alternative scenario for platelet mediated liver regeneration involves transfer of RNA from platelets to hepatocytes as has been recently demonstrated in an *in vitro* model (9). Although platelet influx of the liver remnant shortly after partial hepatectomy has been well established in rodent models, it is yet unknown what triggers platelet accumulation and whether platelets persist in the liver remnant over time.

It has been shown that levels of the platelet adhesive protein von Willebrand factor (VWF) are increased in plasma following a partial liver resection in rats and in mice (21,22). VWF protein is also highly upregulated in liver sinusoidal endothelial cells following a partial hepatectomy (21). Although the latter finding was interpreted as a potential role for VWF in tissue remodeling during liver regeneration, it may also be that VWF release from liver sinusoidal endothelial cells leads to platelet influx into the liver remnant following partial hepatectomy.

In this study we tested the hypothesis that VWF is involved in platelet influx into the liver

CHAPTER 4

remnant. By use of intravital microscopy we studied the dynamics of platelet influx into the liver sinusoids upon partial liver resection in mice. We demonstrated rapid and transient platelet influx into the liver parenchyma after partial liver resection, which was dependent on VWF.

Material & Methods

Partial liver resection in mice

Male C57BL6 mice (Charles River, Leiden, The Netherlands) of 8-10 weeks of age or male mice deficient in VWF (VWF^{-/-}, on a C57BL/6 background(23)) underwent a 70% partial liver resection according to published protocols(24). In sham surgeries, mice underwent an identical procedure with the exception of ligation and removal of the liver lobes. Surgical procedures were performed under isoflurane inhalation anesthesia (Abbott, Chicago, IL). Thrombocytopenia was induced by intravenous injection of a rat monoclonal antibody directed against mouse Gplb α (4 μ g/g body weight) (Emfret, Würzburg, Germany). In selected experiments, 50 μ g of the polyclonal rabbit anti-VWF antibody A0082 (DAKO, Glostrup, Denmark) was intravenously injected 30 minutes prior to resection. The Institutional Animal Care and Use Committee of the University of Groningen, The Netherlands approved these studies.

Mice were terminated by exsanguination from the inferior vena cava after injection of 150 μ l 3.4% sodium citrate (Merck, Germany) diluted in NaCl (0.9%) in the spleen. Collected blood samples were centrifuged at 1400g for 10 minutes (without brake) to obtain plasma and were stored at -80°C. Livers were fixed in 4% formaldehyde or were snap frozen in liquid nitrogen for immunohistochemical analyses.

Confocal intravital microscopy

Platelets were imaged in living mice shortly after the hepatectomy by intravital microscopy as described previously (25). Platelets were labeled *in vivo* by intravenous injection of 1.6 μ g phycoerythrin (PE)-conjugated hamster anti-mouse CD49b (clone HMa2) (BD Pharmingen, San Diego, CA) just prior to an imaging session as described (25). After partial liver resection or sham operation the animal was placed in a right lateral position on an adjustable microscope stage. Mouse body temperature was maintained at 37 °C. After the liver was exteriorized, it was placed on the inverted microscope, the liver surface was covered with a small piece of saline-soaked KimWipe (Kimberly-Clark, Roswell, GA) to keep the organ moist and hold the organ in position. Image acquisition was started as soon as possible and was performed for 1 hour. Alternatively, mice were examined after 4 hours, 1 day or 3 days after the hepatectomy by relaparotomy. We used two different confocal microscope set-ups in this study. The first set-up has been described previously (25). Another set of experiments was performed using an inverted Zeiss LSM 780 NLO microscope (Axio Observer.Z1; Carl Zeiss, Ulm, Germany) equipped with a temperature controlled incubator (XL S1 DARK; Pecon, Erbach, Germany). For these experiments a 20 $\times$ PlnApo, 0.8 NA

TRANSIENT VON WILLEBRAND FACTOR-MEDIATED PLATELET INFLUX STIMULATES LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN MICE

objective was used. Images were captured using 488nm Argon laser and a gallium arsenide phosphide (GaAsP) spectral detector (Carl Zeiss, Ulm, Germany) at 508 nm to 561 nm for autofluorescence detection, revealing the vasculature, and 569 nm to 655 nm for PE-detection. Hardware control was via the ZEN Black acquisition software (Carl Zeiss, Ulm, Germany).

Intravital microscopy image processing and platelet aggregate analysis

For IVM data analysis, tif images were exported from the Volocity (Improvision Inc., Lexington, MA) acquisition software or from ZEN Black software. Images for platelet aggregate quantification were imported directly into ImageJ (version 1.45; US National Institutes of Health) and image contrast was set to maximum for sharp definition of the borders of each platelet aggregate. The same settings were applied to images from all treatment groups within a single experiment. Analysis of platelet aggregates was performed using the Analyze Particles function within ImageJ. Videos underwent contrast enhancement within the acquisition software package, adjusting the Black Point for each fluorescence channel. Again, the same settings were applied to the videos of all treatment groups within a given experiment. Videos were exported as .avi files and were converted to an appropriate size, resolution, and frame rate using Microsoft Movie Maker (Microsoft, San Jose, CA). A platelet aggregate was defined as a positive signal of 10 pixels (1 μ m) or more.

Immunohistochemistry

Deparaffinized liver sections were subjected to antigen retrieval. Ki-67 sections were incubated for 20 minutes in boiling Tris/EDTA buffer, pH 9.0. Endogenous peroxidase was blocked by 3% H₂O₂ for 30 minutes. Sections were incubated with monoclonal rabbit anti-Ki67 antibody (1:200 in TBS + 1%BSA) (Abcam, Cambridge, UK) at 4°C for at least 16h. Next, a secondary peroxidase-conjugated goat-anti-rabbit antibody (1:100, DAKO, Glostrup, Denmark) and a tertiary peroxidase-conjugated rabbit-anti-goat antibody (1:100, DAKO, Glostrup, Denmark) were used. Prior to the incubation with the secondary and tertiary antibody normal rabbit serum (1:100) was added for 30 minutes. The peroxidase activity was visualized by a 10 minute incubation in 3,3-diaminobenzidine tetrachloride (Sigma, St.Louis, MO). Subsequently the sections were counterstained for 1 minute with haematoxylin and mounted with Kaiser's glycerin gelatin. Ki-67-positive hepatocytes were manually counted in at least 5 high-power fields per mouse and expressed as percentage of all hepatocytes.

Statistical analysis

Statistical analysis was performed with the GraphPad Prism 5 (San Diego, CA) software package. Continuous variables were expressed as mean $\pm$ SD or median and range. Values are representative of at least 3 independent experiments performed in triplicate. Continuous data were tested for normality and analyzed by t-test, Mann-Whitney U-test or one-way ANOVA, as appropriate. A P value of less than 0.05 was considered statistically significant.

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Results

Transient platelet influx into the liver remnant immediately after partial liver resection

We studied platelet influx after partial liver resection in mice using intravital microscopy. Following partial liver resection, an immediate platelet influx in the remnant liver was observed (Fig. 1A). Platelets appeared to attach to the endothelial cells and formed both small and larger aggregates in the sinusoid, but the aggregates never became occlusive (Supplementary video 1). The aggregates were unstable as platelets or groups of platelets frequently detached from these aggregates, and continuous reattachment of new platelets was observed. In sham-operated mice some platelets transiently attached to the endothelial cells but the quantity and size of platelet aggregates was substantially less compared to the mice that underwent partial hepatectomy (Fig. 1A, supplementary video 2). Intravital imaging at 4h, 1 day, and 3 days after liver resection showed minimal platelet deposition compared to the early phase (<1h) after liver resection (Fig. 1B, supplementary video 3).

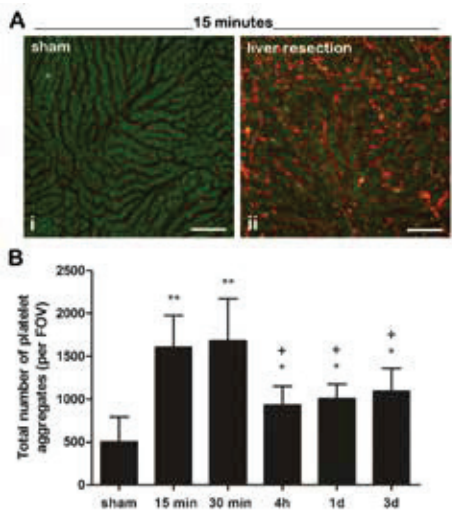


Figure 1: Platelet influx into the liver remnant immediately after partial liver resection

(A) Representative intravital microscopy images of livers of c57/bl6 mice at 15 minutes after a partial liver resection or sham operation. Platelets were labeled in vivo with PE-conjugated anti-CD49 (red). The autofluorescence signal of the liver is displayed to visualize liver anatomy (green). Original magnification 200x. Scale bar denotes 50µm.

(B) Quantification of the total number of platelet aggregates in the sinusoids of the liver remnant. Platelet aggregates were quantified in sham operated mice at 15 minutes after the sham surgery and at different time points after partial liver resection. *P < 0.05, **P < 0.01 versus sham. + P < 0.05 versus 30 min hepatectomy. Data represent the mean of three animals. Error bars indicate SD.

TRANSIENT VON WILLEBRAND FACTOR-MEDIATED PLATELET INFLUX STIMULATES LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN MICE

Transient platelet influx stimulates liver regeneration

To study whether the transient influx of platelets following a partial hepatectomy is sufficient to stimulate liver regeneration, we compared liver regeneration in mice that were rendered thrombocytopenic 2 hours prior to or two hours after a partial hepatectomy. Intravenous injection of platelet-depleting antibodies resulted in a >90% reduction in platelet count within 15 minutes (data not shown). Compared to mice with a normal platelet count, mice that were rendered thrombocytopenic prior to partial hepatectomy showed markedly impaired regeneration as evidenced by a reduced liver/body weight ratio (Fig. 2A) and a reduction in ki67-positive cells at day 3 after partial hepatectomy (Fig. 2B-C). In contrast, liver regeneration was only marginally impaired in mice that were rendered thrombocytopenic 2 hours after partial hepatectomy. Importantly, no excessive perioperative bleeding was observed in thrombocytopenic animals, nor was there evidence of bleeding observed during termination.

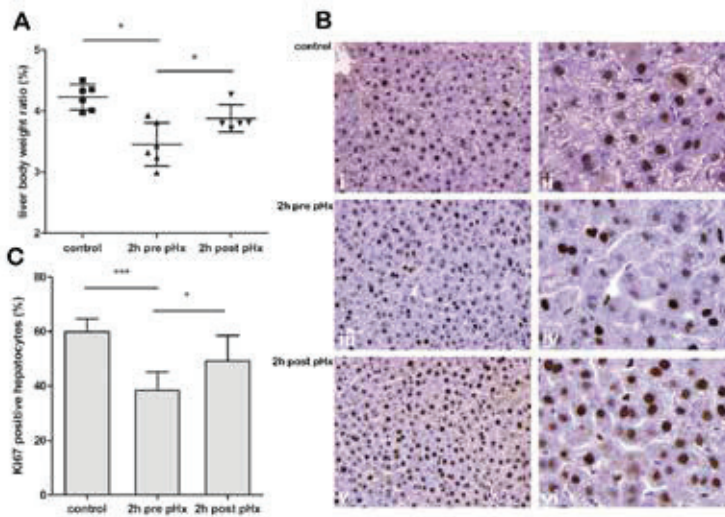


Figure 2: Transient platelet influx stimulates liver regeneration.

(A) Quantification of liver to body weight ratio in mice 3 days after partial liver resection. Thrombocytopenia was induced either 2h prior to or 2h after partial liver resection (pHx) and compared to untreated (control) mice. * $P < 0.05$. Horizontal bars represent means. Error bars indicate SD.

(B) Immunohistochemical staining of Ki-67 on liver paraffin sections. Mice were sacrificed 3 days after partial liver resection. (i, ii) Ki-67 staining on mice with a normal platelet count (i) original magnification 200x, (ii) original magnification 400x, (iii, iv) mice that were rendered thrombocytopenic two hours prior (iii) 200x, (iv) 400x and (v, vi) mice that were rendered thrombocytopenic two hours after partial liver resection (v) 200x, (vi) 400x. Images are representative for six animals.

(C) Quantification of Ki-67-positive hepatocytes in groups represented in (B). *** $P < 0.001$. * $P < 0.05$. Data represent the mean of six animals. Error bars indicate SD.

CHAPTER 4

Platelet influx into the liver is mediated by VWF

To assess the role of VWF in platelet influx into the liver remnant, we blocked VWF function by a polyclonal antibody to VWF and performed intravital imaging of platelets immediately following partial hepatectomy. As shown in figure 3, VWF blockade substantially reduced platelet influx following partial hepatectomy to levels similar to that observed in sham operated mice (Fig. 3A). We observed a significant reduction of the number of platelet aggregates after partial liver resection when VWF was inhibited (Fig. 3B).

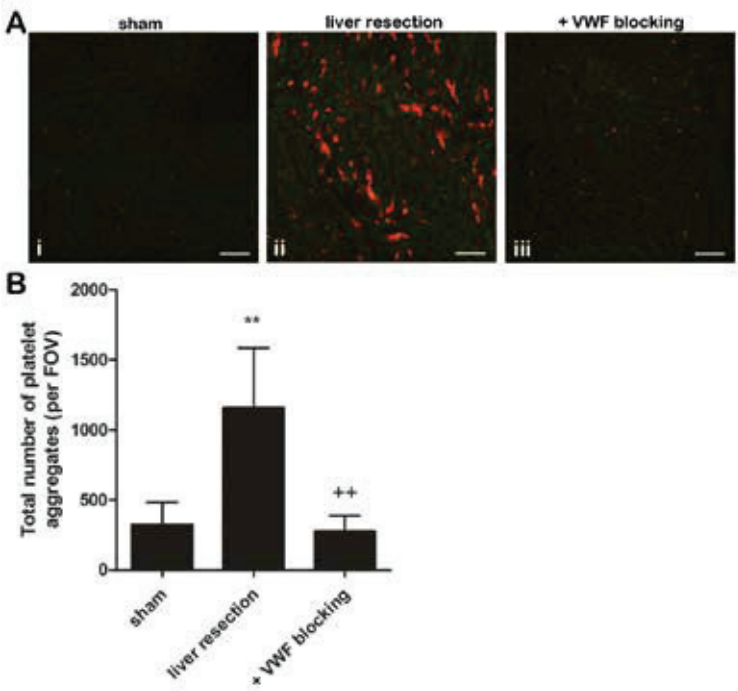


Figure 3: VWF mediates platelet influx into the liver

(A) Representative intravital microscopy images of c57/bl6 control mice or mice treated with an inhibitory antibody to VWF. Platelets were labeled in vivo with PE-conjugated anti-CD49 (red). The autofluorescence signal of the liver is displayed to visualize liver anatomy (green). (i) 15 minutes after sham operation (ii) 15 minutes after partial liver resection (iii) or 15 minutes after partial liver resection in the presence of an inhibitory antibody to VWF. Original magnification 200x. Scale bar denotes 50µm. (B) Quantification of the total number of platelet aggregates in the sinusoids of the liver remnant. Platelet aggregates were analyzed in sham operated mice (n=3), mice that underwent partial liver resection (n=6) and mice that were treated with a blocking VWF antibody prior to partial liver resection (n=6). **P < 0.01 vs sham. ++ P < 0.01 vs liver resection. Error bars indicate SD.

TRANSIENT VON WILLEBRAND FACTOR-MEDIATED PLATELET INFLUX STIMULATES LIVER
REGENERATION AFTER PARTIAL HEPATECTOMY IN MICE

VWF deficiency impairs liver regeneration

As VWF mediates transient platelet influx following partial hepatectomy and transient platelet influx stimulates liver regeneration, we next studied liver regeneration in VWF deficient mice. The liver/body weight ratio was similar in WT and VWF^{-/-} mice at day 1 after partial hepatectomy, but was significantly higher in WT compared to VWF^{-/-} mice at day 3 (Fig. 4A). In line with these results, the proportion of ki-67-positive hepatocytes was substantially higher in WT compared to VWF^{-/-} at day 3 (Fig 4B-C). Importantly, no excessive perioperative bleeding was observed in VWF^{-/-} mice, nor was there evidence of bleeding observed during termination.

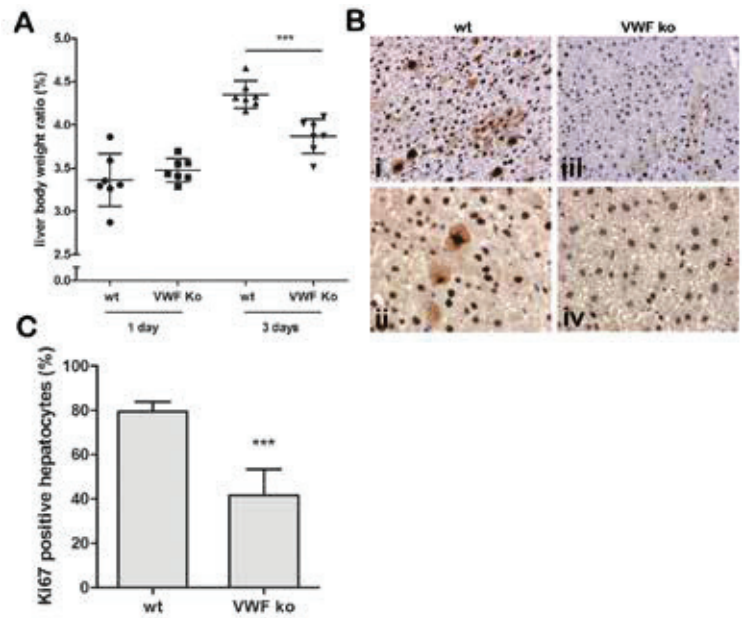


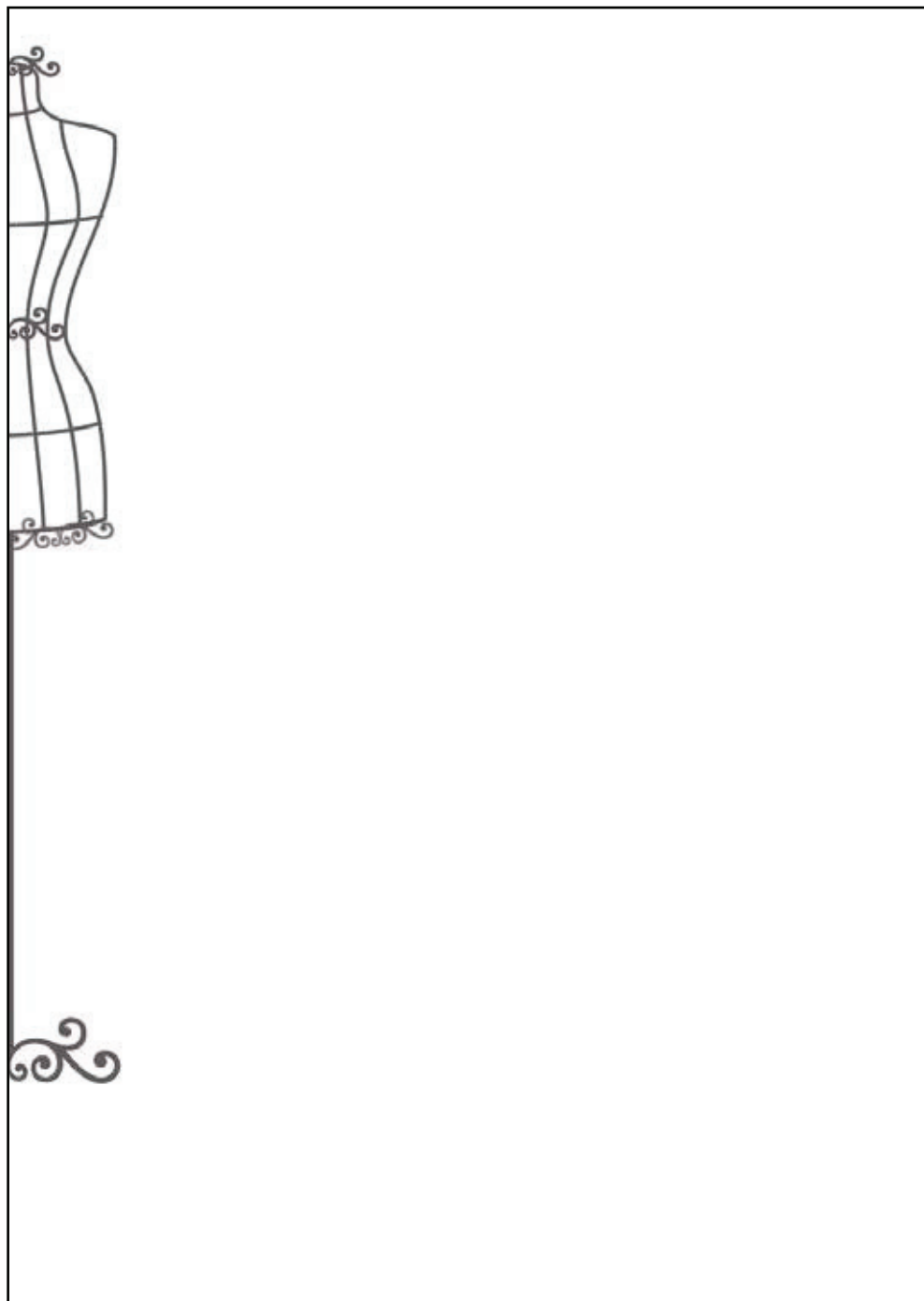
Figure 4: Mice deficient in VWF show impaired liver regeneration

(A) Liver to body weight ratio of WT mice compared to VWF knock out mice at day 1 and day 3 after liver resection. ***P < 0.001. Horizontal bars indicate means. Error bars indicate SD.

(B) Immunohistochemical staining of Ki-67 on liver sections from mice 3 days after partial liver resection. Representative images of Ki-67 staining of WT mice (i) original magnification 200x, (ii) original magnification 400x and of VWF knock out mice (iii) 200x, (iv) 400x.

(C) Quantification of the percentage Ki-67-positive hepatocytes in WT mice and VWF knock out mice at day 3 after partial liver resection. ***P < 0.001. Data represent the mean of seven animals. Error bars indicate SD.

90 GSM BIOTOP



5

Perceptions of self-management in primary care:
a cross-sectional survey study.

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Under review

Abstract

Background: Self-management support is increasingly provided in primary care settings. Perceptions of primary care providers regarding self-management support and of what patient characteristics they think influence the success of self-management support are expected to guide their decisions regarding the extent to which a patient is exposed to self-management.

Objectives: This study aims to explore the perceptions of general practitioners (GPs) and practice nurses (PNs) about self-management support and patient-related factors that can influence the success of self-management support. Furthermore, we will explore differences in perceptions of GPs and PNs.

Method: Between March and June 2014, data was collected through a self-administered online survey set out among primary care providers in the Netherlands.

Results: In total, 272 respondents completed the survey (114 GPs and 158 PNs). The majority of care providers see their role in self-management support as mainly coaching the patient. Most providers aim to stimulate patients to take responsibility for their health behaviour and treatment. Differences between GPs and PNs exist mostly in that PNs more often provide self-management support. Key patient-related factors for successful self-management support, as perceived by both providers, were motivation (93.2%), knowledge of disease (82.6%), educational level (80.4%), self-efficacy (77.2%) and patient-provider relationship (60.3%).

Conclusion: This study provides new insights in perceptions of care providers on self-management support in primary care which can improve and support the implementation of self-management. Furthermore, key patient-related factors influencing success of self-management support were explored. Future studies should evaluate whether these patient factors also influence the decision making of care providers regarding the provision of self-management support.

Introduction

Globally, the number of people with one or more chronic diseases is increasing with huge impact on health care systems worldwide. To safeguard quality, continuity and affordability of care, in the Netherlands and many other countries, chronic care made a gradual transition from secondary to primary care and from primary care to self-care. Also a shift of chronic care from the general practitioner (GP) towards the practice nurse (PN) is taking place. In chronic disease management, self-management support, induced by the chronic care model, has become increasingly important¹. Health professionals provide self-management support to assist the patient in managing their condition². Considering that self-management for patients entails managing the symptoms, treatment, physical and psychosocial consequences and lifestyle changes related a chronic condition³, care providers need knowledge, tools and skills to be able to assess their patients' needs and support them in self-management.

Self-management support is currently embedded in most national and international chronic care guidelines and GPs and PNs both play a key role in self-management support. However, recent studies indicate that self-management is not (yet) an integral part of daily practice and perceptions regarding the provision of self-management support substantially vary between providers^{4,5}. Van Hooft et al. stated that different perceptions of nurses also led to differences in self-management support⁶. Therefore, it is important to know the perceptions of care providers on different aspects of self-management support and what self-management activities are taking place in primary care.

Even though self-management interventions have shown to be effective there is a substantial variance in effectiveness⁷⁻⁹. Therefore, tailoring self-management to the specific needs and preferences of the patient might be the key to effective implementation of self-management support¹⁰. What care providers perceive as important factors for the success of self-management support will influence whether certain patient factors will be assessed and whether self-management support will be provided accordingly. Which patient factors are perceived to be of influence in the success for self-management support and whether there are differences in the perceptions of GPs and PNs is unknown. Other factors such as age and work experience could also influence these perceptions and (clinical) decision making¹¹. Since male and female professionals have different communication styles¹², gender could also be of influence on perceptions of patient-related factors.

Objectives

The primary aim of this study is to explore how GPs and PNs perceive self-management support, more specifically we will explore (1) perceptions about the importance of self-management support, their role in self-management support and their aim with self-

management support, and (2) which self-management activities are currently taking place in practice and which five self-management activities they find most important in self-management support. Furthermore, we will explore which patient-related factors they think influence the success of self-management support. The secondary aim is to explore differences between GPs and PNs in their perceptions of self-management support and whether certain care provider characteristics influence their perceptions on patient-related factors.

Methods

Design and participants

A descriptive cross-sectional study was conducted among general practitioners, final year GP trainees, and PNs working in general practices in the Netherlands. Participants were approached by regional primary health care organizations, the General Practice Specialty Training institutes in the Netherlands and by a mailing from the Dutch Nurses Association. Participants were recruited between March – June 2014.

Data collection

Data was collected through an online questionnaire. The questionnaire was developed for the study purpose by the research team, with scientific and practical expertise in nursing and primary care. Content was based on a thorough review of the literature combined with expert consultation. The questionnaire was pilot-tested by three GPs and three nurses. To assess face and content validity of the questionnaire, they assessed the questions for clarity, relevance, completeness and monitored the time to complete the questionnaire. The validation process did not require substantial changes of the questionnaire, only some practical suggestions were adopted. The questionnaire could be completed within 10 minutes.

In the first part of the questionnaire, several characteristics of the care providers were assessed: sex, age, province, environment (rural/urban), type of practice (single or multiple partner practice), profession, years of work experience and additional relevant courses (i.e. self-management course or motivational interviewing course) followed. Subsequently, three multiple choice questions addressed the care provider's perception of the importance of self-management support, their role in self-management support, and their aim with providing self-management support. Furthermore, they were asked to choose the five most important self-management support components from a list of 19 pre-defined components which are all described in the literature as self-management support component. In addition, they were asked to indicate the extent to which these activities are applied in clinical practice: 'never'; 'sometimes'; 'most of the time' or 'always'. In the final part, care providers were asked to choose (from a list of 15 factors) patient-related factors they thought would influence the success of self-management

support. Subsequently, they ranked the five most important factors from 1 to 5, where 1 represented the most important factor.

Data analysis

The chi-square test was used for analysing differences between GPs and nurses. Logistic regression analyses were performed to explore whether provider characteristics (gender, age, work experience, profession and practice type) influence the perception of the importance of patient factors for the success of self-management. Depending on the mean and the distribution of the number of respondents, the cut-off point for age was determined based on the median age of the care providers. Comparisons with a p-value <0.05 were considered statistically significant. All statistical procedures were performed using SPSS version 22.0 for Windows¹³.

Results

A total of 272 respondents completed the questionnaire, including 114 GPs and 158 nurses (response rate approximately 10%). Of the 114 GPs 23% were final year GP trainees. Table 1 provides an overview of the baseline characteristics.

Table 1. Baseline characteristics of participating general practitioners and practice nurses.

	General practitioner (n=114)	Practice nurse (n=158)
Gender		
Male	49 (43.0%)	6 (3.8%)
Female	65 (57.0%)	152 (96.2%)
Age	47.2 ± 11.7	46.0 ± 10.2
Years in function	16.0 ± 10.6	7.3 ± 4.3
Years working in patient care		23.1 ± 10.7
Practice type		
Single	28 (24.6%)	41 (25.9%)
Duo	40 (35.1%)	44 (27.8%)
Group	46 (40.4%)	73 (46.2%)
Practice location		
Big city (>100.000 citizens)	37 (32.5%)	32 (20.3%)
City (30.000-100.000 citizens)	36 (31.6%)	52 (32.9%)
Small city (10.000-30.000 citizens)	24 (21.2%)	51 (32.3%)
Small town (<10.000 citizens)	17 (14.9%)	23 (14.6%)
Training in motivational interviewing	25 (21.9%)	111(70.3%)
Self-management course	9 (7.9%)	58 (36.7%)

GP= General practitioner, PN= practice nurse

Perceptions of self-management support regarding importance, care providers' role and their aims

The majority of care providers stated that self-management support was important for the quality of chronic care (GPs 64%, PNs 52.5%, *p*-value 0.19), results are shown in Table 2. On asking how care providers consider their role in supporting self-management, the majority thought their role was mainly coaching (GPs 59.6% and PNs 65.2%, *p*-value 0.16). The main aim with providing self-management respondents reported as giving the patient an active role and responsibility in his/her treatment and health behaviour (GPs 56.1%, PNs 73.3%, *p*-value 0.03). However, nurses provided self-management support more often with the aim to give the patient an active role and responsibility in treatment and health behaviour than GPs. GPs more often than nurses stated that their aim with self-management support is to ameliorate the quality of life and the quality of care for patients.

Table 2. Perceptions of self-management support regarding importance, care providers' role and their aims

	Total N (%)	GPs N (%)	PNs N (%)
How do you feel about self-management support in chronic care?			
I think it is important to improve the quality of chronic care	156 (60%)	73 (64%)	83 (57%)
I think it is important in reducing the workload	3 (1%) 85 (33%)	2 (2%) 30 (26%)	1 (1%) 55 (37%)
I think it is important for certain patients but not for all patients	16 (6%)	9 (8%)	7 (5%)
I think the importance of self-management support is overrated.			
As care provider you can have different roles in supporting self-management to a patient. How would you consider your role?			
Mainly to educate/inform patients	55 (21%)	26 (23%)	29 (20%)
Mainly to coach patients	180 (69%)	73 (64%)	107 (73%)
Mainly to motivate patients	25 (10%)	15 (13%)	10 (7%)
What is your main aim with providing self-management support?			
To improve health outcomes and quality of life of patients	70 (27%)	39 (34%)	31 (21%)
Providing effective care (e.g. reducing hospital admissions or reducing consultation number)	12 (5%) 171 (66%)	6 (5%) 64 (56%)	6 (4%) 107 (73%)
To give the patient an active role and responsibility in his/her treatment and health behavior	3 (1%) 4 (1%)	3 (3%) 2 (2%)	0 (0%) 2 (2%)
I do not have a main purpose, I follow the current trend			
I do not provide self-management support			

GP= General practitioner, PN= practice nurse

Most often applied components of self-management support

Self-management components that were stated to be applied in practice are shown in Table 3. Nurses apply most self-management components more often than GPs except for providing a delayed prescription. Additionally, we asked which 5 components of this list care providers perceived as most important in self-management support. For GPs the 5 most frequently mentioned components were increasing understanding of the disease (59.6%), helping patients take ownership in their care (52.6%), establishing common goals with respect to treatment (52.6%), encouraging patients to adjust medication dosage guided by symptoms (43.0%), and stimulating medication adherence (40.4%). Nurses perceived the following components as most important: increase understanding of the disease (71.5%), establish common goals with respect to treatment (60.1%), help patients take ownership of their care (46.8%), teach required skills to the patient (46.8%) and apply motivational interviewing (38.6%).

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Table 3. Frequency of self-management components that are performed in clinical practice

<i>Self-management activities</i>		<i>never</i>	<i>sometimes</i>	<i>usually</i>	<i>always</i>
Increase understanding of the disease*	GP	1%	3%	48%	48%
	PN	0%	1%	23%	76%
Encourage smoking cessation	GP	1%	6%	50%	43%
	PN	0%	3%	43%	54%
Encourage exercising*	GP	1%	9%	59%	31%
	PN	0%	1%	43%	56%
Stimulating medication adherence*	GP	2%	10%	63%	25%
	PN	0%	2%	28%	70%
Encourage diet adherence*	GP	2%	21%	60%	17%
	PN	0%	7%	49%	44%
Encourage self-recording measured values*	GP	2%	23%	62%	13%
	PN	3%	12%	49%	36%
Make the patient responsible for contacting the GP or nurse in case of problems	GP	3%	26%	49%	22%
	PN	1%	19%	49%	31%
Establish common goals with respect to the treatment*	GP	5%	34%	53%	8%
	PN	0%	23%	59%	18%
Encourage self-monitoring of symptoms	GP	4%	28%	58%	10%
	PN	3%	25%	50%	22%
Apply motivational Interviewing*	GP	4%	53%	39%	4%
	PN	1%	20%	65%	14%
Teach required skills to the patient*	GP	8%	48%	35%	9%
	PN	1%	23%	52%	25%
Give information brochures	GP	4%	35%	50%	11%
	PN	0%	38%	51%	11%
Help patients take ownership of their care*	GP	6%	50%	39%	5%
	PN	2%	35%	53%	10%
Create responsibility for making regular follow-up appointments	GP	7%	43%	39%	11%
	PN	9%	47%	39%	5%
Encourage patients to adjust medication dosage guided by symptoms	GP	7%	65%	25%	3%
	PN	8%	54%	31%	7%
Encourage use of E-health	GP	19%	56%	25%	0%
	PN	26%	58%	14%	2%
Give delayed prescription*	GP	11%	75%	12%	2%
	PN	69%	27%	3%	1%
Offer self-management workshops/courses*	GP	67%	26%	7%	0%
	PN	51%	43%	5%	1%
Organize group interventions and consultations aimed at self-management	GP	74%	23%	3%	0%
	PN	74%	22%	3%	1%

GP= General practitioner, PN= Practice nurse *Statistically significant difference between GPs and PNs in frequency of applying self-management support component

Patient-related factors

Patient-related factors that were perceived as important factors for success of self-management support are shown in Figure 1. The top 5 ranking of factors were (1) motivation, (2) knowledge of the disease, (3) education level, (4) self-efficacy and (5) patient-provider relationship. On average, care providers considered almost eight patient factors to be of influence on self-management success (GPs considered a mean of 8.3 factors and PNs 7.5 factors to be of influence). Furthermore we explored whether certain provider characteristics would be of influence on which patient factors they think will influence the success of self-management (Table 4). Profession had the highest impact on the choice for certain patient factors, while practice type did not influence their choice. Males consider knowledge of disease and self-efficacy as less important than females, younger care providers think social support is less important than older care providers, and care providers with <5 years of work experience are more likely to think that age is an important factor and think that self-efficacy is less important than care providers with more work experience.

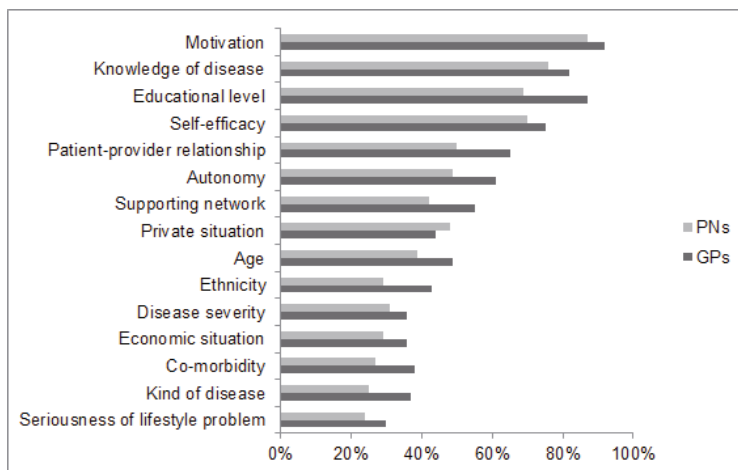


Figure 1. Patient-related factors that influence the success of self-management support according to primary care providers

Table 4. Logistic regression of how care provider characteristics influence the perception of the importance of patient factors for the success of self-management.

Patient factors	Provider characteristics	OR (CI)
Knowledge of the disease	GP vs. PN	2.7 (1.2-6.1)
	Male vs. female	0.2 (0.1-0.6)
Educational level	GP vs. PN	2.9 (1.5-5.5)
Self-efficacy	GP vs. PN	1.9 (1.0-3.8)
	Male vs. female	0.4 (0.2-0.8)
	<5 yrs experience vs. >5 yrs experience	0.5 (0.3-0.9)
Patient-provider relationship	GP vs. PN	1.8 (1.1-3.0)
Autonomy	GP vs. PN	1.8 (1.1-3.0)
	Younger vs. older age	0.6 (0.4-1.0)
Supporting network	GP vs. PN	1.7 (1.0-2.8)
	Younger vs. older age	0.5 (0.3-0.8)
Age	<5 yrs experience vs. >5 yrs experience	2.8 (1.6-4.9)
Ethnicity	GP vs. PN	1.9 (1.1-3.1)
Co-morbidity	GP vs. PN	1.6 (1.0-2.8)
Kind of disease	GP vs. PN	2.4 (1.3-4.4)

OR= Odds ratio, CI= confidence interval. The model included 5 provider characteristics: profession (GP=general practitioner vs. PN=practice nurse), gender (male vs female), age (younger than median age vs older), Work experience in current profession (<5 years experience vs > 5 years), practice type (solo vs. group practice).

Discussion

This study found that two-third of the primary care providers share their perceptions regarding the importance of self-management support, and their aim and role in providing it. Overall, most self-management activities are more often applied by nurses. The most important patient-related factors for successful self-management support as perceived by all care providers are motivation, knowledge of disease, educational level, self-efficacy, and patient-provider relationship.

The majority of care providers stated that self-management is important for the quality of chronic care. About a third stated that it is important for a subgroup of patients but not for everyone. These opinions correspond with current evidence from meta-analyses that showed that quality of chronic care is indeed improved and that self-management is associated with positive results in certain patients but certainly not in all patients⁷⁻⁹. The role care providers play in self-management support was by the majority perceived as mainly coaching while a minority thought their role was to educate or to motivate the

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