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► **To cite this version:**

Per Hjerpe, Henrik Ohlsson, Ulf Lindblad, Kristina Bengtsson Boström, Juan Merlo. Understanding adherence to therapeutic guidelines: a multilevel analysis of statin prescription in the Skaraborg Primary Care Database. *European Journal of Clinical Pharmacology*, 2010, 67 (4), pp.415-423. 10.1007/s00228-010-0973-4 . hal-00655423

HAL Id: hal-00655423

<https://hal.science/hal-00655423>

Submitted on 29 Dec 2011

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Understanding adherence to therapeutic guidelines: a multilevel analysis on statin prescription in the Skaraborg Primary care database

Per Hjerpe, MD ^{1,2}, Henrik Ohlsson, PhD ², Ulf Lindblad, MD, PhD ³, Kristina Bengtsson
Boström, MD, PhD ¹, Juan Merlo, MD, PhD ²

1) R&D Centre, Skaraborg Primary Care, Skövde, Sweden

2) Social Epidemiology, Department of Clinical Science, Faculty of Medicine, Lund
University, Sweden

3) Department of Public Health and Community Medicine/Primary Health Care, The
Sahlgrenska Academy at Gothenburg University, Sweden

Reprint requests and correspondence to

Per Hjerpe, MD

FoU-centrum Primärvården Skaraborg

Storgatan 18

S-541 30 Skövde, Sweden

E-mail per.hjerpe@vgregion.se

Telephone +46500478594

Fax +46500478598

Abstract

Purpose: In Skaraborg, Sweden the economical responsibility of tax-financed drug cost was transferred from the regional administration to the local HCC in the year 2003. The aim of this study was to investigate the impact of the decentralization of the economic responsibility on adherence to guidelines on prescription of lipid lowering drugs.

Methods: From the Skaraborg Primary Care Database (SPCD) with data from all 24 public health care centres (HCC) in Skaraborg, prescriptions of lipid lowering drugs during 2003 and 2005 were extracted. Multilevel regressions analysis (MLRA) was used to disentangle the variances at different levels of the data (patient, physician, HCC). The outcome variable on the patient level was prescription of recommended statin (y/n). Sex and age of the patients and sex, age and occupational status of the physician was included as fixed effects. The variance was expressed as Median Odds Ratio (MOR).

Results: The prevalence of adherence with guidelines for prescription of statins increased from 77 % in 2003 to 84 % in 2005. The MLRA showed that in 2003 the variance was equally distributed between HCC and physician levels ($MOR_{HCC2003} = 1.89$ vs. $MOR_{PHYSICIAN2003} = 1.88$) in 2003. The variance between physicians and between HCCs decreased considerably between 2003 and 2005. The inclusion of individual and physician characteristics did not explain any of the remaining variance.

Conclusion: The decentralized budget seemed to increase adherence to guidelines and reduce inefficient variation in prescribing.

Keywords

- Primary Health Care
- Medical Records Systems, Computerized
- Drug Prescriptions
- Multilevel Analysis
- Quality Assurance, Health Care

Introduction

The use of prescription guidelines aiming to implement general therapeutic standards is today a common feature in many health care systems [1]. The need for guidelines arises from a general understanding that promoting evidence based and efficient medical care may reduce unnecessary medical practice variation and improve quality [2]. Moreover guidelines may also be an aid for prescribers that are hardly able to assimilate the increasing volume of new scientific information [1, 3-5]. Even though the investigation of adherence to guidelines is attracting increasing interest, it is still not sufficiently understood what and how factors at different levels of the health care organization condition adherence to guidelines [6-9].

In Sweden, every county council has a therapeutic committee responsible of the issuing of evidence-based guidelines [10, 11]. Despite these recommendations several studies have demonstrated substantial and unexplained differences in the adherence with guidelines among physicians and among Health Care Centres (HCC) [8, 9, 12, 13]. These differences might express themselves as a clustering of similar prescription behavior among physicians at the same HCC and suggest the existence of local therapeutic traditions. Quantifying and understanding this variation is relevant for the planning of interventions aimed to improve the

quality of drug prescription.

In the Region of Skåne, Sweden, the implementation of a decentralised drug budget increased adherence to guidelines and promotes efficient drug therapy [9]. Similarly, in Skaraborg, Sweden the economical responsibility of tax-financed drug cost was transferred from the regional administration to the local HCC in the year 2003. However, the effects of this intervention are still unknown. In the present study, using multilevel regression analyses, and data from the Skaraborg Primary Care Database (SPCD) [14] we evaluate the effect of this decentralised drug budget. We focus on adherence to statin (HMG-CoA reductase inhibitors) prescription since this group of cholesterol lowering drugs has very homogeneous indications and similar efficacy which nearly eliminates the possibility of confounding by indication and patient mix when comparing different practices and physicians. We also aimed to disentangle the relevance of different levels (i.e. patients, physicians, HCCs) for understanding adherence with guidelines. Based on previous studies [9] our hypothesis was that the decentralized budget would result in an increased prevalence and a decreased variance between physicians and between HCCs, concerning prescription of recommended statins.

Materials and Methods

The Skaraborg Primary Care Database (SPCD)

Skaraborg, one of four administrative areas of the region of Västra Götaland in the southwest of Sweden is mostly rural and it is inhabited by approximately 250 000 individuals within 15 municipalities. Inpatient care is offered by three public hospitals and primary care by 24 public and one private HCC as well as by a few private solo practitioners. About 250 000 office visits are registered at the public HCCs every year. Approximately 75% of all drug prescriptions are issued outside the hospitals and 85% of them at public HCCs.

The SPCD started in 2000 and is based on a common computerized medical journal used by all the 24 publicly administrated HCCs in the area. Among other information all drug prescriptions, laboratory tests, and current diagnosis at every consultation are recorded. The SPCD allows the identification of the HCC, the physician and the patient by a unique anonymized identification number.

Study population

From the SPCD, we identified all patients with at least one prescription of statin defined according to the Anatomical Therapeutic Chemical (ATC) classification system code C10AA [15]. Thereafter we selected two datasets, (i) patients with at least one statin prescription during May 2002 to October 2003 (i.e., 2003 dataset, n=7460), and (ii) during July 2004 to December 2005 (i.e., 2005 dataset, n=9643). If a patient received more than one statin prescription during each time period, the last one was selected. Prescriptions for other cardiovascular drugs, Long-acting nitrates (ATC codes: C01DA08, C01DA14), Loop diuretics (C03C), Potassium-sparing diuretics (C03D), Diuretic combinations (C03E), Thiazides (C03A, C03B), Beta blockers (C07), Calcium channel blockers (C08), ACE-inhibitors (C09A, C09B), Angiotensin receptor blockers (C09C, C09D), Fibrates (C10AB), and Resins (C10AC) were also extracted. In order to identify homogeneous physician-patient relations, only patients with all his/her cardiovascular drugs issued by the same physician were included, resulting in 6205 patients, treated by 425 physicians at 24 HCCs in the 2003 dataset and 7979 patients treated by 402 physicians at 24 HCCs in the 2005 dataset.

Individual level variables

The outcome variable was prescription of recommended statin (yes v. no). In the 2003 dataset, these drugs were Simvastatin (Zocord® or generic simvastatin) and Pravastatin (Pravachol®) and in the 2005 dataset only Simvastatin (Zocord® or generic simvastatin). We categorized

the age of the patients into four age groups: <54 years, 55-64, 65-74, and 75-, and used the youngest group as reference in the comparisons. We included the sex of the patients as a dummy variable using women as reference in the analysis. Based on the actual evidence neither age nor sex or any other patient characteristic should motivate the preferential prescription of a specific statin before any other. Therefore, the inclusion of individual-level variables in the analysis was not motivated by the need of adjustment for confounding but rather, because we wanted to gain an understanding of the importance of these factors in the prescribing process.

Physician level variables

Previous studies have shown that prescription behaviour is influenced by prescriber characteristics. We, therefore, included physician's occupational status categorized as Intern (IN), Resident (RS), General practitioner (GP) or Locum (LOC). Each category was split into two groups according to the median age of the specific group (Table 1). Of the eight different groups older GPs were used as reference in the analysis. We included the sex of the physician as a dummy variable using women as reference in the analyses. However, information on physician's characteristics was only available for the 2005 dataset.

Multi-level regression models

We used multilevel logistic regression analysis [16, 17] to estimate the probability of prescribing a recommended statin, while accounting for the hierarchical structure of the data (i.e., patients nested within physicians nested within HCCs). We developed three consecutive models (A, B, C) for data set 2003 and 4 models (A, B, C and D) for data set 2005. Model A was an empty two level model including only patients and HCCs as random effects. Model B was a three-level model in which patients were nested within physicians that were in turn nested within HCCs. Model C and Model D added the patient characteristics respectively patient and physician characteristics. In this way we aimed to investigate if the individual and

contextual characteristics could explain the residual variation between physicians and between HCCs. We estimated odds ratios and 95 % credible intervals (95 % CI) from the models. Model fit was evaluated by comparing change in the deviance information criteria (DIC).

In the random-effects part of the multilevel analysis, we obtained the variance and 95% credible intervals at the physician and the HCC levels and used this information to calculate the median odds ratio (MOR) and 95% credible intervals [16-19]. The MOR translates the variance into the odds ratio (OR) scale, and is thereby comparable with OR of individual or area variables. The MOR can be interpreted as the amount by which a randomly selected patients odds of receiving a recommended statin would increase (in median) if this patient moved to a physician/HCC with higher adherence to guidelines. If the MOR was equal to 1, there would be no differences between physicians or HCCs in the odds of prescribing a recommended statin. If there were important physician-level or HCC differences, the MOR would be large on this level.

We calculated the percentage of change in magnitude of variance (PCV) that was explained between the initial (references) model ($\text{Var}_{\text{initial}}$) when including more variables in an extended model (Var_{more}):

$$\text{Percentage of change (PCV)} = ((\text{Var}_{\text{initial}} - \text{Var}_{\text{more}}) / (\text{Var}_{\text{initial}})) \times 100$$

We used this percentage to estimate the relevance of the individual and contextual characteristics for understanding a possible clustering of prescriptions of recommended statins. Parameters were estimated by Markov chain Monte Carlo (MCMC) methods with the MLwiN 2.00 software [20].

We also calculated the absolute change in variance (CV) between the two time periods (2003 and 2005) and a t-test was performed to calculate their 95% confidence intervals (CoI).

Change in variance (CV) = $\text{Var}_{2005} - \text{Var}_{2003}$

The study was approved by The Regional Ethical Review Board in Gothenburg.

Results

Table 1 indicates that overall the prevalence of adherence with guidelines for prescription of statins increased from 77 % in 2003 to 84 % in 2005 (Relative Ratio: 1.09 (95% CoI, 1.01 – 1.19)). In 2003 older patients had higher adherence to guidelines, but these age differences disappeared in 2005. Men were prescribed statins more often than women, but there were no gender related differences in the prescription of recommended drugs. In 2005, 68% of all the statins were prescribed by male doctors who also showed a slightly lower percentage of prescription of recommended statins than female colleagues. Young intern physicians showed the highest (90%) and older locums the lowest (77%) adherence with guidelines.

Figure 1 illustrates that although there were some HCCs with rather low adherence to guidelines in 2003 all HCCs had approximately 80 % adherence in 2005. It is also obvious that the HCCs with the poorest adherence in 2003 showed the largest improvement in 2005.

Multi-level regression analysis

Table 2 shows the association between on the one hand patient and physician characteristics and on the other prescription of recommended statins according to the multilevel regression analysis. In 2003 adherence to guidelines increased with age of the patients, but in 2005 there

were no differences between age groups. Older locum physicians presented a lower probability of prescribing a recommended statin than older GPs

Model A in table 3, only includes two levels (i.e., patients and HCCs) and shows that in median a randomly selected patient's odds of receiving a recommended statin would increase 2.14 times in 2003 ($MOR_{HCC2003} = 2.14$) and 1.37 times in 2005 ($MOR_{HCC2005} = 1.37$) if he/she moved to an HCC with higher adherence to guidelines.

Model B in table 3 includes three levels and shows that the HCC and physician levels accounted each for approximately 50 % each of the variation at the higher levels in 2003 ($MOR_{HCC2003} = 1.89$ vs. $MOR_{PHYSICIAN2003} = 1.88$). In 2005 the variance among HCCs and physicians was lower ($MOR_{HCC2005} = 1.30$ vs. $MOR_{PHYSICIAN2005} = 1.52$). From 2003 to 2005 the variance between physicians and between HCCs decreased by 55 % and 82% respectively.

The inclusion of patient and physician characteristics (Models C and D) did not have an influence on the variance at the different levels. Figure 2 illustrates that in 2003 about 30% of the HCCs and approximately 4% of the physicians differed from the overall mean adherence while in 2005 none of the HCCs and only a few physicians differed conclusively from the overall mean.

Discussion

Our investigation demonstrates that transferring the economical responsibility from the central health care authorities at the County Council to the local HCCs seems to have improved adherence to statin prescription guidelines. The use of recommended statins increased from 77 % in 2003 to 84 % in 2005 and the variance among HCCs and among physicians decreased. Our results fully agree with a previous analysis performed in the county of Scania [9]. However, the current analysis also adds information regarding the physician

level. We show that approximately 50 % of the higher level variance could be attributed to the physician level, which is in line with other studies [21]. In 2005, after the decentralized budget, the differences between HCCs and between physicians became almost negligible and therefore the possibility to distribute the variance to different levels of analysis was limited. This is also illustrated in figure 2 by the fact that none of the HCC and only a few physicians conclusively differed from the overall mean adherence in 2005.

While our analytical approach of focusing on both changes in variance and changes in prevalence has been implemented in other research fields [22-24] it has rarely been used for investigating practice variation in pharmacoepidemiology. Observing an increase in the prevalence of prescription of recommended statins does not necessarily imply an improvement since the variation around the prevalence could be very high. The desired outcome is obviously not only to increase adherence with guidelines but also to eliminate unnecessary practice variation.

An advantage of the multilevel regression analysis is that it allows disentangling the variance in the outcome among the different levels of analysis and using this information for identifying which level could be most relevant for a possible intervention. In 2003 the variance at the higher levels was rather large and equally distributed among HCCs and physicians, indicating that any intervention aimed to improve adherence with guidelines should be focused on both levels simultaneously. The decentralized budget, that was implemented, was a general intervention towards all HCCs and all physicians that was disseminated through the HCCs. Still it appeared to effectively decrease the variance at both levels. However, an intervention directed towards specific HCCs and physicians would theoretically also be effective in reducing variance. In 2005 the higher level variance was very small which suggests that any further intervention directed towards specific HCCs or physicians would render less effective.

In 2005 we observed that older locum physician had a lower adherence to prescription guidelines than older GPs, which may reflect intrinsic characteristics of this personal category. Locum physicians share the common work environment and the same constraints as other physicians at the HCC but only for a limited period of time and therefore might be less affected by the therapeutic traditions acting at the HCC. However, an intervention focusing on locums will possibly not be very efficient [25] since the variance at the physician level (and the corresponding MOR) was negligible. Observational epidemiological studies are often the only option for investigating questions that for practical, economical, or ethical reasons cannot be analysed by randomized trials [26-29]. Confounding and selection bias may threaten the validity of the studies. However, because of similar indications and efficacy, statins are an ideal medication group for investigating prescribing behaviour [30], and there is no rationale for considering patient characteristics as confounding factors when investigating practice variation. The value of including individual and physician covariates resides in the understanding of the prescription process. In the present investigation we only considered basic individual variables such as age and gender of the patient, and our results showed that for dataset 2003 younger patients had a lower propensity to receive recommended statins. This circumstance cannot be justified by any medical argument, but may rather reflect the influence of constructed social roles and expectations. From the perspective of equity in health care, it is relevant to question the physicians' choice of more expensive, but not more efficient, brands for some groups of patients, given that a large part of this medication expenditure is funded by the public reimbursement system. We can not exclude that unmeasured factors besides the decentralized budget might have influenced the observed results (i.e., increase in prevalence and reduction in variance). In addition, the expiration of the Zocord patent in 2003, with the following decline in price for generic simvastatin and increase in cost difference with other statins, might have contributed in choosing the

recommended statin. Information campaigns issued by the local therapeutic committee and the growing awareness of rising costs for medication are other possible contributing factors. Most patients receive statins as a long time therapy. However, according the Swedish law, a prescription can not be issued for a period longer than one year. Therefore, in routine care repeat prescriptions are sometimes issued by phone and eventually by a different physician. We have tried to identify homogeneous physician-patient relations by only including patients with all cardiovascular prescriptions by the same physician. However, we can not exclude a delayed effect of the decentralized budget conditioned by the fact that new users are prescribe recommended drugs, but for continuous users change to recommended drugs are slow, especially if the repeated prescription is written by another physician.

Our study investigates statin prescription in primary health care. Therefore, our results are not directly applicable to those drug prescribed for patients at hospital care. Older patients treated in municipal homecare are also excluded since their prescriptions are not registered in the database. On the other hand, a study of statin treatment in a local community in Skaraborg showed that very few old (85 or more years) used statins [31].

The period of analyses was relatively short so it can not be excluded that an immediate positive response is followed by a later gradual return to the pre intervention situation. Therefore, in order to obtain some information on the effect of the intervention beyond 2005 we also analysed the prevalence of recommended statins in the time period from July 2008 to December 2009. Because at the moment of the analyses this data was not complete (i.e., it included only 23 out of 24 HCCs and there was not information on prescribers) we did not include it in the main multilevel analysis. This analysis indicated that the overall prevalence of recommended statin prescriptions in 2008-2009 was 89%, which suggest that the effects of the intervention were stable (analyses available on request).

Practice variation is a common phenomenon that is not necessarily inappropriate but rather may reflect different therapeutic approaches confronting a similar health problem [32].

However, when the same pharmacological therapy is available as different brands at different prices and the prescriber selects the more costly, there are reasons to question the suitability of the observed practice variation.

In conclusion, our study suggests that decentralization of the drug budget to the HCCs, i.e., transferring the economical responsibility and the power in management and decision-making to the HCCs, seemed to be an appropriate intervention for reducing inefficient therapeutic traditions. As a natural consequence, adherence to the drug committee's recommendations increased and differences between physicians and between HCCs decreased.

Acknowledgements

This research was funded by the Skaraborg research and development council, Skaraborg primary care research and development council, and the Skaraborg Institute, Skövde, Sweden. The Swedish Research Council (Juan Merlo, Dnr 2004-6155 and The Centre for Economic Demography), the Swedish council for working life and social research (Juan Merlo, Dnr: 2007-1772), by an ALF Government Grant Research program (Juan Merlo, Dnr M: B 39 977)

Conflict of Interest

The authors declare that they have no conflict of interest.

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Figure legends

Fig. 1 Prescription of statins, for the 24 health care centres in Skaraborg included in the analysis

Top panel, X-axis; the percentage of recommended statins 2003. Y-axis the percentage of recommended statins 2005

Bottom panel .X-axis; percentage of recommended statins in 2003. Y-axis the differences of prescriptions (percentage) between 2003 and 2005

Fig. 2a Residuals from the multilevel regression analysis of statin prescriptions for the different levels (health care centres/physicians) in Skaraborg 2003

Fig. 2b Residuals from the multilevel regression analysis of statin prescriptions for the different levels (health care centres/physicians) in Skaraborg 2005

Tables

Table 1. Characteristics of the patients cared by only one physician in relation to the prescription of recommended statins in the Skaraborg Primary Health Care Database (SPHD). Values are number of patients (percentage) if not other indicated

	2003		2005	
	Yes	No	Yes	No
Patient variables				
Individuals	4772 (77)	1433 (23)	6719 (84)	1260 (16)
Age: min-max, (mean years)	30-89 (66)	31-89 (64)	18-93 (66)	25-104 (66)
-54	637 (73)	233 (27)	855 (84)	166 (16)
55-64	1465 (75)	497 (25)	2009 (83)	404 (17)
65-74	1710 (78)	471 (22)	2354 (85)	424 (15)
75-	960 (81)	232 (19)	1501 (85)	266 (15)
Men	2498 (76)	779 (24)	3603 (84)	660 (16)
Women	2274 (78)	654 (22)	3116 (84)	600 (16)
Physician variables (Age)				
			Number of physicians	
Young intern (-29)	-	-	21	113 (90)
Old intern (30-)	-	-	22	91 (82)
Young resident (-34)	-	-	32	420 (85)
Old resident (35-)	-	-	29	306 (83)
Young general practitioner (-49)	-	-	65	2419 (84)
Old general practitioner (50-)	-	-	64	2910 (85)
Young locum (-46)	-	-	89	243 (82)
Old locum (47-)	-	-	80	217 (77)
Men	-	-	271	4568 (84)
Women	-	-	131	2151 (86)

Table 2. Association between on the one hand patient and physician characteristics and on the other prescription of recommended statins in 2003 and 2005 according the multilevel regression analysis on the Skaraborg Primary Health Care Database (SPHD). Measures are Odds ratios (OR) and 95% credible intervals (95% CI)

	Model C		Model D
	2003 OR (95% CI)	2005 OR (95% CI)	2005 OR (95% CI)
Patient characteristics			
Age group			
-54	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
55-64	1.05 (0.84-1.29)	0.96 (0.78-1.17)	0.95 (0.77-1.16)
65-74	1.32 (1.08-1.62)	1.07 (0.88-1.30)	1.06 (0.86-1.29)
75-	1.51 (1.20-1.89)	1.09 (0.87-1.35)	1.07 (0.86-1.33)
Sex (men vs. women)	1.01 (0.88-1.14)	1.07 (0.95-1.22)	1.08 (0.95-1.23)
Physician characteristics			
Young interns	-	-	1.67 (0.78-3.43)
Old interns	-	-	0.85 (0.48-1.58)
Young residents	-	-	0.91 (0.62-1.32)
Old residents	-	-	0.80 (0.55-1.18)
Young GPs	-	-	0.87 (0.69-1.10)
Old GPs	-	-	1.00 (Reference)
Young locum physicians	-	-	0.75 (0.51-1.11)
Old locums physicians	-	-	0.56 (0.38-0.82)
Sex (men vs. women)	-	-	0.87 (0.71-1.07)

Model C is a three level (patients, physicians and HCCs) analysis including HCC and physician as random intercepts and patient characteristics as fixed effects. **Model D** develops model C by also including physician characteristics

Table 3. Analysis of variance of prescription of recommended statins obtained from the multilevel regression analysis in the Skaraborg Primary Health Care Database (SPCD) in the years 2003 and 2005.

	Model A		Model B		Model C		Model D
	2003	2005	2003	2005	2003	2005	2005
Variance							
HCC (Intercept)							
Variance (95 % CI)	0.64 (0.33-1.16)	0.11 (0.04-0.23)	0.44 (0.20-0.88)	0.08 (0.02-0.20)	0.46 (0.20-0.91)	0.07 (0.01-0.19)	0.06 (0.00-0.16)
MOR	2.14 (1.73-2.80)	1.37 (1.22-1.58)	1.89 (1.53-2.44)	1.30 (1.12-1.52)	1.92 (1.54-2.49)	1.29 (1.10-1.51)	1.26 (1.07-1.47)
Physician (Intercept)							
Variance (95 % CI)	-	-	0.44 (0.30-0.60)	0.20 (0.12-0.30)	0.44 (0.31-0.62)	0.20 (0.12-0.30)	0.21 (0.13-0.31)
MOR	-	-	1.88 (1.68-2.10)	1.52 (1.40-1.68)	1.89 (1.70-2.12)	1.53 (1.39-1.69)	1.54 (1.40-1.70)
HCC & Physician (Intercept)							
Variance (95 % CI)	-	-	0.88	0.28	0.90	0.27	0.27
MOR	-	-	2.45	1.66	2.47	1.64	1.64
Proportional Change in variance (PCV)							
Between models			From model A		From model B		From model B
HCC	-	-	-31%	-27%	-4.5%	12.5%	25%
Physician	-	-	-	-	0%	0%	-5%
Change in variance (CV)							
Between years							
HCC (95 % CoI, %)	-0,53 (-0,88 - -0,18)	-83%	-0.36 (-0.65 - -0.07)	-82%	-0.39 (-0.68 - -0.10)	-85%	-
Physician (95 % CoI, %)	-	-	-0.24 (-0.32 - -0.16)	-55%	-0.24 (-0.32 - -0.16)	-55%	-
Goodness of the fit							
DIC (MCMC)	6157.85	6898.25	5947.56	6803.07	5936.96	6806.30	6805.55

HCC: Health Care Centre, MOR: Median Odds Ratio, DIC: Diagnostic Information Criteria, MCMC: Marcov Chain Montecarlo

Model A is a two level analysis (patients and HCCs) that includes only HCC as a random intercept. **Model B** is a three level (patients, physicians and HCCs) analysis including HCC and physician as random intercepts. **Model C** is analogous to model B but includes patient characteristics as fixed effects. **Model D** develops model C by also including physician characteristics

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