vitos Rheingau

Voraus//gedacht 2016

3. Platz

Vitos Klinikum Rheingau
KPP Eichberg

Ärztliche Direktorin
Prof. Dr. Sibylle C. Roll

Matching pharmacy care to patients with mental illness

LWV Hessen

ESCP Belfast Oct 26th 2018
11:30-12:30

Prof. Dr. Martina Hahn, PharmD

vitos Rheingau

Agenda //

- Background: what are the patients needs?
- The „Eichberger Model“
- Pharmaceutical care services in a psychiatric hospital to
  - Increase Drug safety
  - Improve response and avoid side effects by the use of Pharmacogenetics in psychiatry
- Financial considerations for a clinical pharmacist in hospitals
- Take home message

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BACKGROUND

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Why psychiatry / patients with mental illness? //

- 1. There is a high risk for relevant drug interactions and drug related problems in psychiatry due to the pharmacokinetic and pharmacodynamic profile of the psychotropic drugs

Arzneistoff	Enzyme und Transporter
Acamprosat	keine Metabolisierung
Agomelatin	CYP1A2, CYP2C19, CYP3A4
Alprazolam	CYP3A4/5
Amantadin	90 % werden unverändert über die Niere ausgeschieden
Amisulprid	Mehr als 80 % werden unverändert über die Niere ausgeschieden
Amitriptylin	CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4, UGT1A3, UGT1A4, UGT2B15, P-gp (ABCB1)
Amitriptylinoxid	Flavinmonooxygenase, CYP2C19, CYP2D6
Amphetamine (Dimesylat, Sulfat, Lisdexamfetamin)	CYP2D6
Aripiprazol	CYP2D6, CYP3A4, P-gp (ABCB1)
Asenapin	CYP1A2, UGT1A4
Atomoxetin	CYP2C19, CYP2D6, P-gp (ABCB1)
Benzodiazepine	Unklar

Arzneistoff	Enzyme und Transporter
Diazepam	CYP2B6, CYP2C19, CYP3A4, UGT2B7, P-gp (ABCB1)
Diphenylpropylamin	CYP3A4
Diphenylsulfone	CYP2D6, UGT1A1, UGT2B10, P-gp (ABCB1)
Disulfiram	CYP1A2, CYP2A6, CYP2B6, CYP2E1, CYP3A4
Donepezil	CYP2D6, CYP3A4, P-gp (ABCB1)
Duloxetin + Terbinafin	CYP2C19, CYP1D6
Escitalopram	CYP2C19, CYP2C19, CYP2D6
Fluoxetin	Unklar
Gabapentin	CYP2C9, CYP3A4, UGT1A3, UGT1A4, UGT1A8, UGT1A10
Haloperidol	CYP1A2, CYP2D6, P-gp (ABCB1)
Ketamin	UGT1A9
Lacosamid	CYP2C19, CYP2D6, CYP3A4, P-gp (ABCB1)
Ethanol	Alkoholdehydrogenase, CYP2E1
Naltrexon	Renale Exkretion

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Why psychiatry / patients with mental illness? //

2. Few counselling in retail pharmacy according to many patients, probabaly mainly due to a stigmatization of psychotropic drugs and mental illnesses and a lack of privacy in this setting

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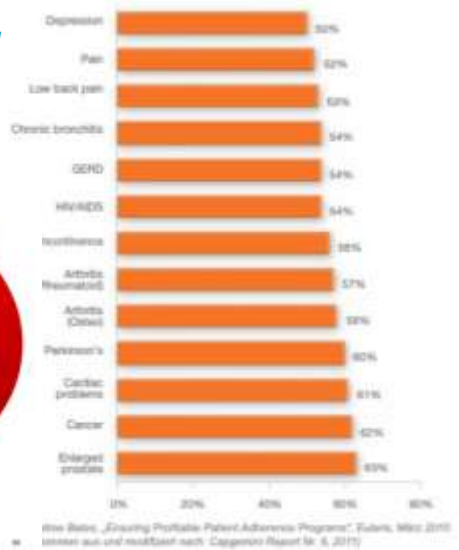
Why psychiatry / patients with mental illness? //

3. Adherence rate is the lowest among all diseases



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Why psychiatry / patients with mental illness? //

- 4. Physician provides prescriptions and psychotherapy: conflicts can arrise
  - A pharmacist can help to overcome these conflicts by counseling the patient about the drug therapy, alternative options etc.

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Background on counselling //

- Psychotherapy = 50 Minutes/week covered by insurance companies
- Precious time, not to be „wasted“ by talking about side effects or selection of drug -> counselling by a pharmacists is a very much appreciated offer
- Also: pharmacist is perceived as a „second opinion“-> patient accepts recommendation (acceptance rate 98,6%).

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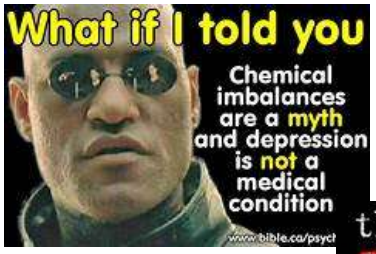
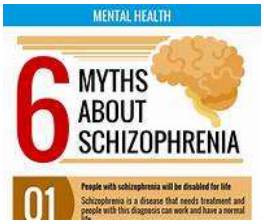
Why psychiatry / patients with mental illness? //

- 5. Lots of myths about psychotropic drugs, especially on „Dr. Google“





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Patient fears psychotropic drugs //

- 6. Common fears about the presciption of pschotropic drugs
  - „They cause addictions“
  - „They cause a change of my personality“
  - „They make me feel „dull““
  - „They cause weight gain“
  - „If I didn´t tolerate one psychotropic drug, I won´t tolerate any other“

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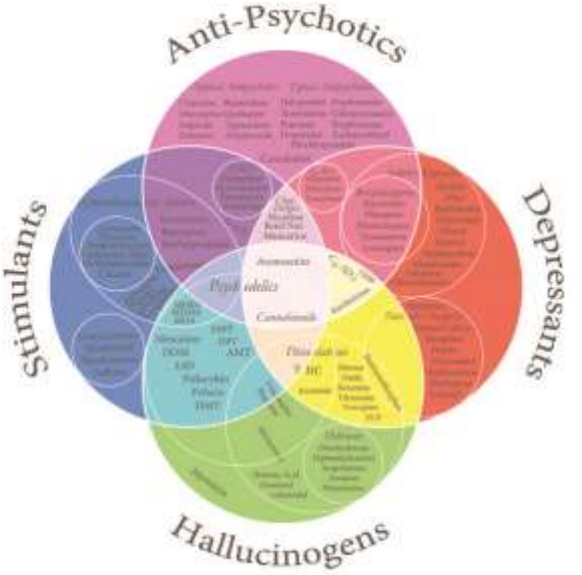
Need for Counselling //

- An individualized counselling is needed, which is time consuming- in times of a lack of physicians
- pharmacists can „fill in“ and provide a very profound counselling on the pharmacology of the drugs



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Educational differences //

- Pharmacist
  - Focus on:
    - Chemistry
    - Pharmacology
    - Technology
- Physician
  - Focus on:
    - Anatomy
    - Pathophysiology
    - Diagnostic and therapeutical issues

By a cooperation we can generate a higher drug therapy safety and better outcomes for our patients

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EICHBERGER MODEL //

Vitos Klinik Eichberg- psychiatric hospital for adults //

- 145 patient beds with 7 units
  - ICU, depressive disorders, trauma and anxiety, geriatrics, addiction, psychosis, personality disorders)
- 40 day care clinic patients
- 3 ambulatory care clinics
- No hospital pharmacy (supplier 20 km from the hospital)

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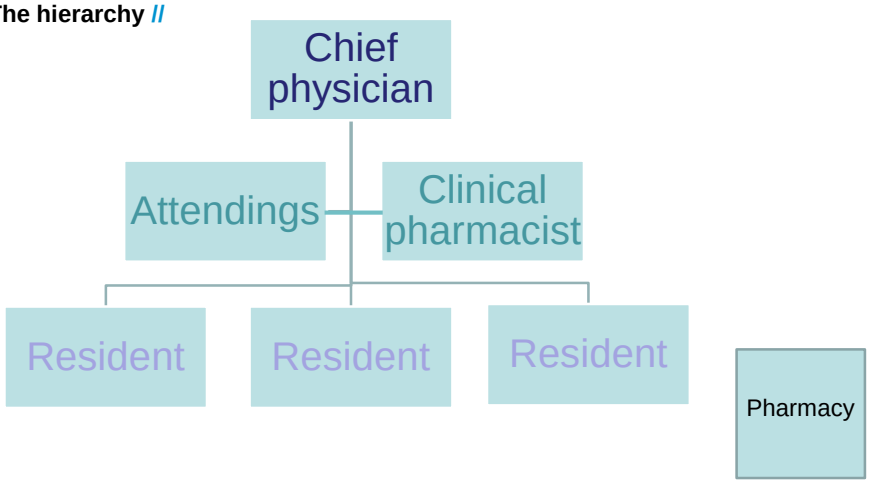
The hierarchy //



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„Eichberger Model“//

The implementation was started in 2011 and took 9 month

1. • Pharmacist attends ward rounds
2. • Pharmacist advices physicians on specific drug interactions and drug therapy problems
3. • Pharmacist helps physicians select and interpret TDM
4. • Pharmacist counsels patients on drug therapy: detects drug related problems and educates patient about drug therapy
5. • Pharmacist establishes medication standards in cooperation with the attendings and chief physician
6. • Pharmacist establishes transmural care (defined as Pharmacist transfers information to outpatient setting)
7. • Pharmacist provides consultation times to reconcile medications and counsels patients
8. • Pharmacist develops standardized documentation for pharmaceutical services in the electronic pt documentation
9. • Pharmacist shares the experience and establishes academic standards

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Psychoeducational groups //

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Psychoeducational groups //

- Modules about antidepressants, antipsychotics, anxiolytics, hypnotics, mood stabilizers, alcohol abuse, drug abuse, nicotine abuse.
- Exchange of information between the patients, guided by a pharmacist
- Our experience shows: patients aksk questions that they would never ask the physician (the pescriber!)
- About 5 groups/week with 5-25 patients each

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Validation of pharmacist–physician collaboration in psychiatry: the Eichberger-model

Requests to the pharmacist (n=147)? //

Table 1 Classification and frequency of the email requests sent by physicians of the psychiatric hospital to the clinical pharmacist

Reason for request	Frequency	
	n	%
Appropriate drug selection	46	31.3
Drug-drug interactions	37	25.2
Adverse drug reactions	25	17.0
Changes in drug therapy	18	12.2
Drug dosing	9	6.1
Therapeutic drug monitoring	7	4.8
Appointment for patient counselling requested by physician	3	2.0
Drug utilisation	2	1.4

n = number of requests in each category; % relative frequency of requests in each category based on a total of n = 147 requests

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Acceptance rate //

	Häufigkeit	
	n	%
Umsetzungen	**145**	**100**
Beibehaltene Umsetzungen	143	98,6
Für zwei Wochen beibehaltene Umsetzungen	139	95,9
Bis Entlassung beibehaltene Umsetzungen, wobei Behandlungszeitraum < zwei Wochen	4	2,8
Nicht beibehaltene Umsetzungen aufgrund patientenspezifischer Eigenheiten	2	1,4

n = Anzahl der beibehaltene Umsetzungen; % = Häufigkeit in Prozent bezogen auf die 145 umgesetzten pharmazeutischen Empfehlungen

Pharmacist and psychiatrist working together= good outcome for the patient

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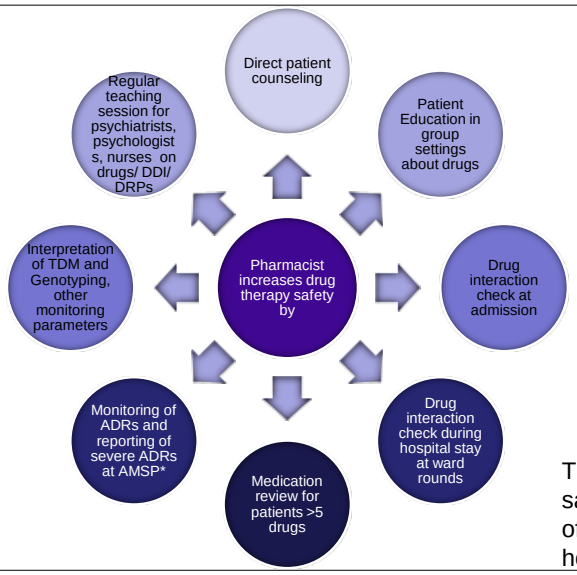

This need for patient safety is not met in most of german psychiatric hospitals at the moment

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IMPACT OF PHARMACEUTICAL CARE IN PSYCHIATRY//

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DRUG THERAPY SAFETY //

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Results of the Pre-Study in a psychiatric hospital (from 2016, n=2.791)

- Presciption of potentially inadequate medication in the elderly (43,9 %)
- No therapeutic Drug-Monitoring of substances with a recommendation level 1 (strongly recommended) according to the AGNP guideline (27,5 %)
- Relevant pharmacokinetic drug drug interactions (17,6 %)
- Combination of 2 or more drugs with a strong QTc-prolonging potential (16,5 %)
- Polypsychopharmacotherapy (5 or more drugs) (13,3 %)
- Combination of 2 or more serotonergic drugs (8,5 %)
- Combination of 2 or more anticholinergic drugs (4,6 %)

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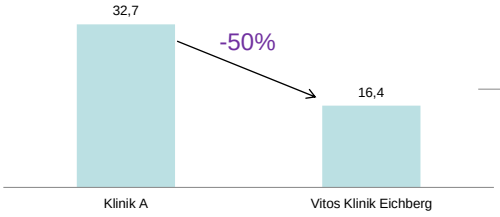
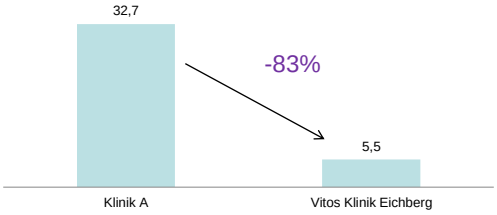
Comparison of the Eichberger Model (n=69) and standard of care (n=62) //

Percent of patiente taking 2 QTc-prolonging drugs [%]



Percent of patients taking 2 or more anticholinergic drugs [%]



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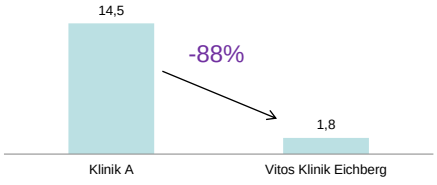
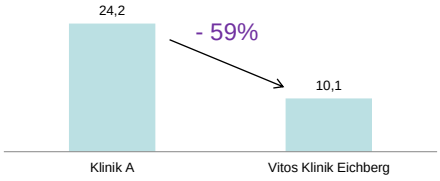
Comparison of the Eichberger Modell (n=69) vs. Standard of care (n=62) //

Percent of patients taking serotonergic drugs [%]



Percent of patients taking more than 4 psychotropic drugs [%]



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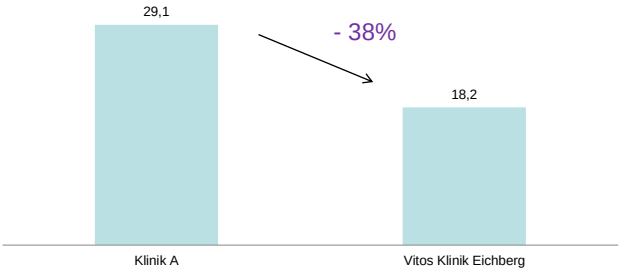
Comparison of the Eichberger Modell (n=69) vs. Standard of care (n=62) //

Percent of patients taking Cyp Inhibitors or inducers (moderate and strong only) [%]



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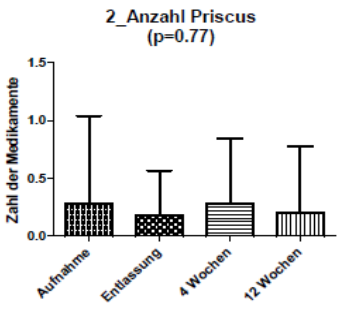
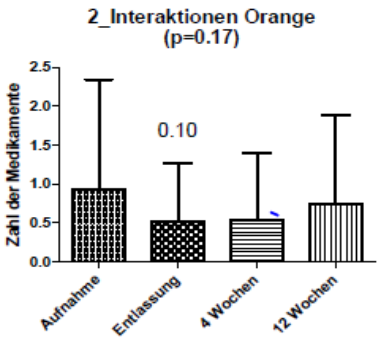
Arzneimitteltherapiesicherheit an der stationär-ambulanten Schnittstelle

Arzneimitteltherapiesicherheit gerontopsychiatrischer Patienten an der Schnittstelle stationär-ambulant //

- n=41 gerontopsychiatric patients over 65 yo.
- 101 pharmaceutical interventions during ward rounds





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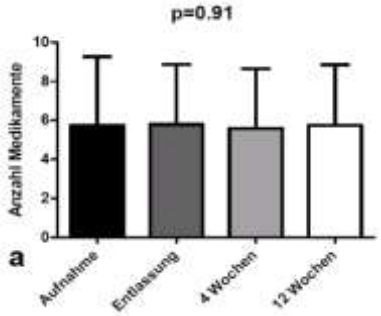
Arzneimitteltherapiesicherheit an der stationär-ambulanten Schnittstelle

Arzneimitteltherapiesicherheit gerontopsychiatrischer Patienten an der Schnittstelle stationär-ambulant //



The pharamcists can help the physician in the selection of drugs and by that avoid drug interactions and the prescirbing of PIMs.

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FKZ 01VSF16009

OSA-PSY: Optimierung der stationären Arzneimitteltherapie bei psychischen Erkrankungen

OSA-PSY //

- Research grant 800.000 Euro
- Analyse the status quo of drug therapy in psychiatry
  - 30.000 patients/year
  - Implement a computerized tool to help the prescriber at the step of prescribing to
    - Avoid drug interactions
    - Define monitoring parameters
    - Avoid contraindications
  - Comparison pre and post implementation

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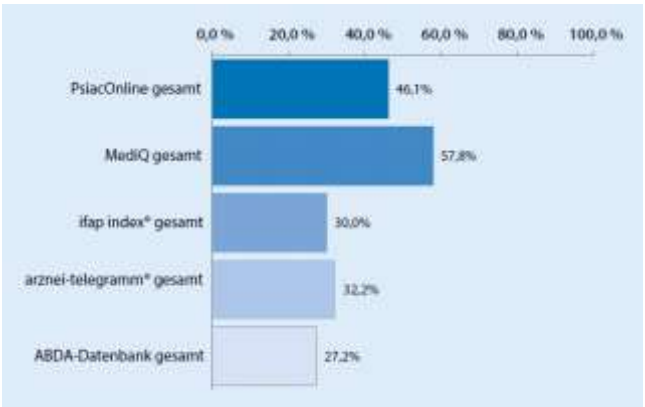
Drug interaction databases //



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Next Step of OSA-Psy //

- To avoid under and over alerting 2 pharmacists and 3 physicians defined important alerts regarding
  - Pharmakokinetic drug interactions
  - Pharmacodynamic drug interactions
  - PIMs
  - Monitoring parameters
- The system is using patient information (e.g. Qtc time, drug levels) for the algorithm, so that overalerting is avoided.

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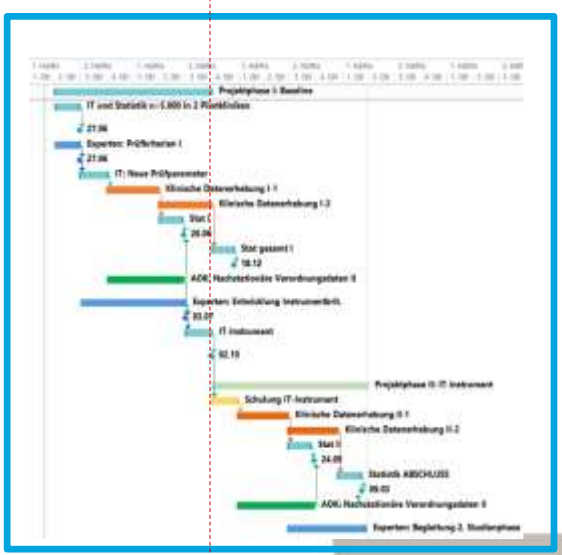
01.04.2017 – 31.03.2020 //



GENOTYPING //

A new field for the clinical pharmacist: Stratified Psychopharmacotherapy //

- Start of using genotypising results to guide psychopharmacotherapy at the Vitos Klinik Eichberg was November 2016
- A pharmacist can
  - Counselling about the genotyping
  - Help interpreting the results and give a recommendation to the psychiatrist about drugs therapy
  - Inform the patient about the genotyping results

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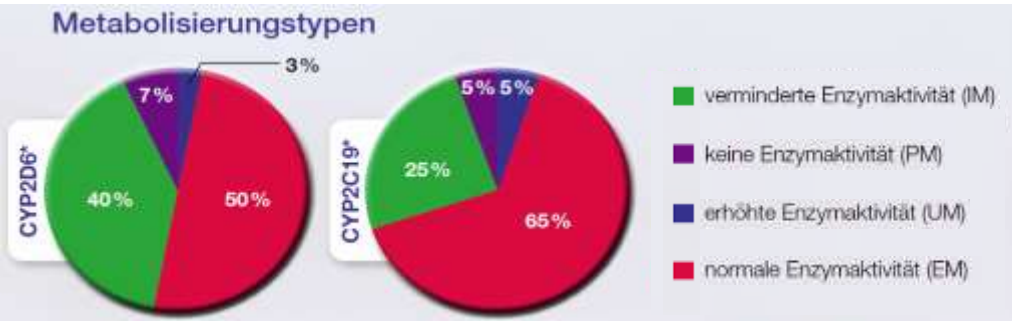
Why is genotyping important in antidepressive drugs? //

- Metabolism mainly by **CYP2C19** and **CYP2D6**, where genetic polymorphisms exist.



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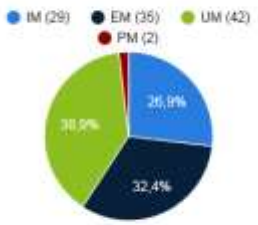
Examples from the Vitos Klinik Eichberg //

CYP2C19

WIRKTYPEN (4)	PATIENTEN (108)	VERTEILUNG
IM	29	26,9%
EM	35	32,4%
UM	42	38,9%
PM	2	1,9%



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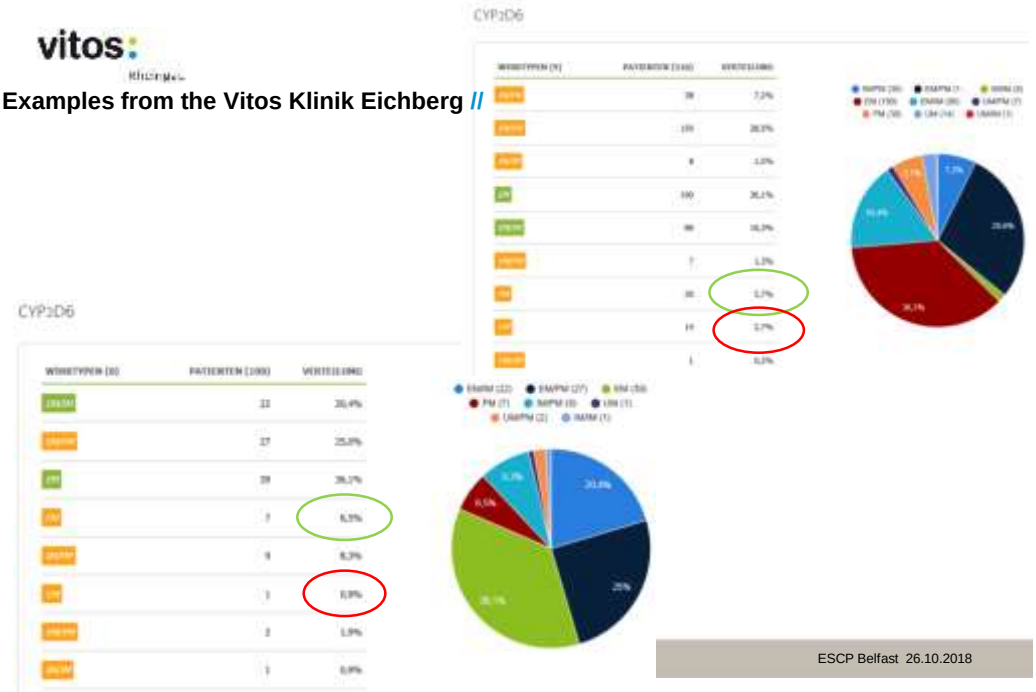
Examples from the Vitos Klinik Eichberg //



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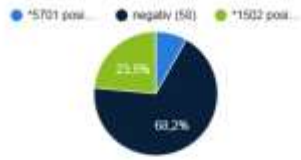
Ergebnisse der Genotypisierung //

HLA-B

WIRKTYPEN (3)	PATIENTEN (108)	VERTEILUNG
*5701 positiv	7	6,5%
negativ	58	53,7%
*1502 positiv	20	18,5%



High risk for Steven Johnson Syndrom in 25% of the patients!

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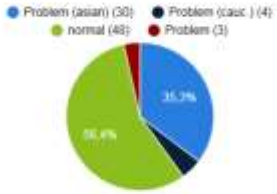
Ergebnisse der Genotypisierung //

HLA-A

WIRKTYPEN (4)	PATIENTEN (108)	VERTEILUNG
Problem (asian)	30	27,8%
Problem (casc.)	4	3,7%
normal	48	44,4%
Problem	3	2,8%



High risk for 3,7% of the caucasian patients, 27,8% in asians

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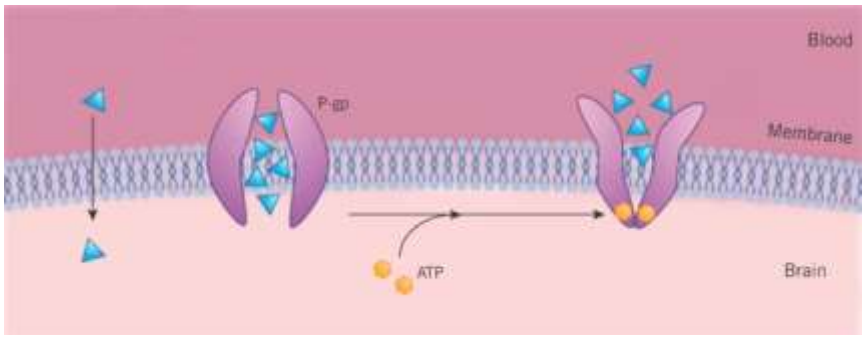
ABCB1-Polymorphism: response rates //



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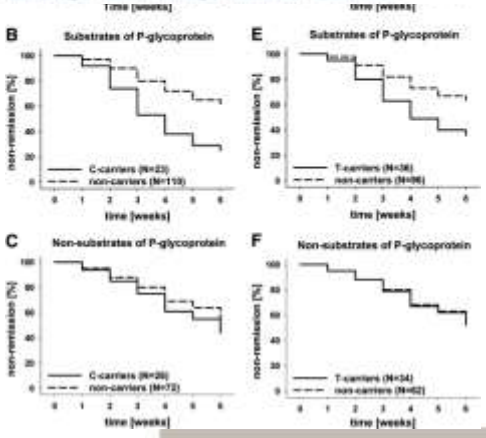
Volume 57, Issue 2, 24 January 2008, Pages 203–209

Clinical Study

Polymorphisms in the Drug Transporter Gene *ABCB1* Predict Antidepressant Treatment Response in Depression

Manfred Uhr[1], Alina Tontsch[1], Christian Namendorf[1], Stephan Ripke[1], Susanne Lucae[1], Marcus Ising[1], Tatjana Dose[1], Martin Ebinger[1], Marcus Rosenhagen[1], Martin Kohli[1], Stefan Kloiber[1]



Examples for Pg-P Substrates:
SSRI und Tricyclics, Milnacipran und Venalfaxine

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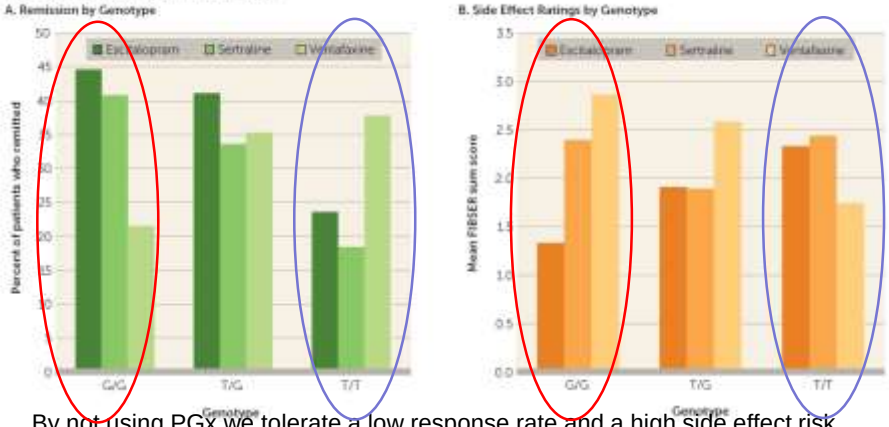
ABCB1 Genetic Effects on Antidepressant Outcomes: A Report From the iSPOT-D Trial

Alan F. Schatzberg, M.D., Charles DeBattista, M.D., Laura C. Lazzeroni, Ph.D., Amit Etkin, M.D., Ph.D., Greer M. Murphy, Jr., M.D., Ph.D., Leanne M. Williams, Ph.D.

FIGURE 2. Interaction of ABCB1 rs10245483 Genotype With Remission and Side Effect Ratings, by Antidepressant Medication, in the Modified Intent-to-Treat Sample (N=683)[a]



By not using PGx we tolerate a low response rate and a high side effect risk

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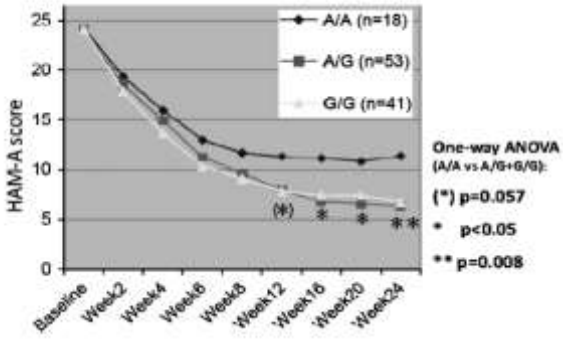
Serotonin receptor 2A (HTR2A) gene polymorphism predicts treatment response to venlafaxine XR in generalized anxiety disorder

5HT2a- Polymorphism and response rates //



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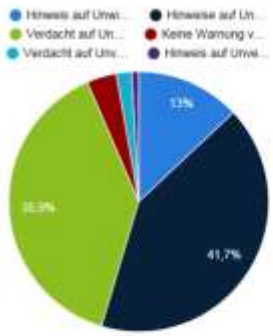
Citalopram

<< Cisplatin >> Clobazam Wirkstoffliste

Gesamtwarnungen

WARNTEXTE (6)	PATIENTEN (108)	VERTEILUNG
	14	13,0%
	45	41,7%
	42	38,9%
	4	3,7%
	2	1,9%
	1	0,9%



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Venlafaxin

<< Vareniclin >> Verapamil Wirkstoffliste

Gesamtwarnungen

WARNTEXTE (4)	PATIENTEN (108)	VERTEILUNG
[redacted]	53	49,1%
[redacted]	46	42,6%
Keine Warnung vorhanden	8	7,4%
[redacted]	1	0,9%

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Warnmeldungen gesamt //

WARNSTUFEN (4)	ANZAHL (30240)	DURCHSCHNITT PRO PATIENT	VERTEILUNG
[redacted]	58	0,5	0,2%
[redacted]	2155	20,0	7,1%
[redacted]	14147	131,0	46,8%
[redacted]	13880	128,5	45,9%

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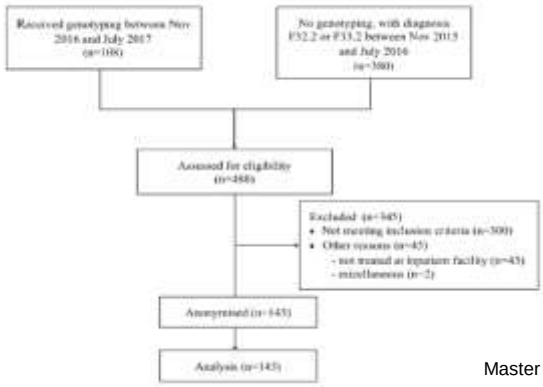
Study design:Retrospective Evaluation of Pharmacogenetics in the Treatment of Major Depressive Disorder- a naturalistic study //



Master Thesis V. Bättig 2018

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The study cohort (n=143, Intervention: n=49, control: n=94) is described in Tab. 1.

Table 1: Description of the intervention and control group

		Intervention	Control	*p*-Value
Group size [n =]		49	94	
Age mean [years] (SD)		41.27 (14.15)	44.12 (16.65)	0.309[a]
Diagnosis, n (%); *expected*	F33.2	42 (85.7); *38.7*	71 (75.5); *74.3*	0.156[b]
	F32.2	7 (14.3); *10.3*	23 (24.5); *19.7*	
Sex, n (%); *expected*	Female	23 (46.9); *25.0*	50 (53.2); *48.0*	0. 478[b]
	Male	26 (53.1); *24.0*	44 (46.8); *46.0*	
History, n (%); *expected*	No stay	24 (49.0); *23.0*	43 (45.7); *44.0*	0. 458[b]
	One stay	12 (24.5); *9.6*	16 (17.0); *18.4*	
	Two stays	5 (10.2); *4.1*	7 (7.5); *7.9*	
	Three or more	2 (4.1); *3.4*	8 (8.5); *6.6*	
	Outpatient	6 (12.2); *8.8*	20 (21.3); *17.1*	
History of therapy with anti-depressants, n (%); *expected*	Not prescribed before (AD-History 1)	11 (22.4); *12.3*	25 (26.6); *23.7*	0. 027[b]
	Replacing existing (AD-History 2)	31 (63.3); *24.0*	39 (41.5); *46.0*	
	Prescribed in the past (AD-History 3)	7 (14.3); *12.7*	30 (31.9); *24.3*	

[a] Student's *t*-Test, [b]Pearson's χ^2

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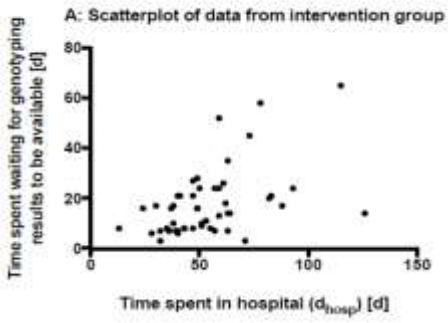
Time until genotypising results were available //



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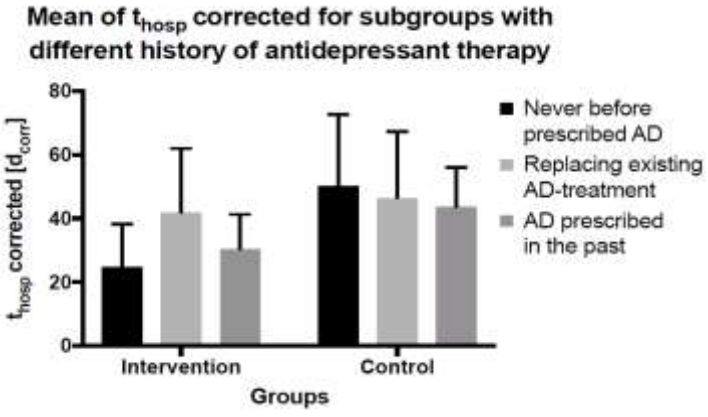
Length of stay subgroup analysis //



Treatment naïve: 24.7 d (±13.5 d); control: 50.2 d (±22.5 d); $p < 0.001$).

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Rehospitalizations //

- Interventions group: 0.16 (0.43)
- Controll group: 0.20 (0.43) p=0.607 (CI= -0.19 - 0.11)
- Intervention group contained more chronically ill patients (85% vs. 75%), so this is a positive trend, even if not statistically significant.

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Financial outcomes of a clinical pharmacist in psychiatry //

Finanzierung der Stelle der klinischen Pharmazeutin über	Gesamt [€]	Anteil ambulant [€]	Anteil stationär [€]
Erlösgenerierung ambulant	246584,-	246584,-	
Einsparung stationär	47038,-		47038,-
Einsparungen der Arzneimittelkosten stationär	18137,-		18137,-
Abzüglich Bruttopersonalkosten TVÖD	106901,-	80% Stellenanteil 89776,-	20% Stellenanteil 17125,-
Gesamt Einsparungen/Erlöse	**204858,-**	**156807,-**	**48050,-**

Presented at the conference on patient safety Berlin 2018

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Take home messages //

- Patients with mental illness need pharmaceutical care to improve the adherence, overcome the stigma, increase drug therapy safety and therfore achieve a good outcome
- A good cooperation between the pharmacist and the psychiatrist is crucial to achieve this
- By a statified therapy side effects can be reduced, response rates increased and so the patient´s suffering can be ended faster, especially in treatment naive patients
- A clinical pharmacist is financially beneficial for the hospital/ ambulatory care clinic, but insurances need to implement reimbursment of clinical pharmacists in the hospital

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Thank you

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