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A new paradigm with old challenges? Ethical implications of personalized medicine

DAAD Science tour at Ludwig-Maximilians-University München

High Tech Campus Martinsried, December 05, 2011

Personalized medicine – a „new“ paradigm?!

PM: field with (analytically) no clear boundary ⇨ object of inquiry??

(Preliminary) definition:

Personalized (or individualized) medicine tries to identify individual (molecular biological) factors that allow to better predict risk of disease and intended/unintended effects of interventions.

Goal:

Prevention, diagnostic, prognostic and therapy tailored to the individual

De facto: patient subgroups ⇨ *stratified medicine*

Ethical Implications

Methodological Challenges

- Not clearly defined, very heterogeneous field

➪ *individual adjustment of considerations necessary*

- Early stage of development: „visions“, but no broad practical application yet

➪ *anticipative technology assessment*

- “PM is in” – hype about PM

➪ *realistic assessment of possibilities of PM necessary*

➪ *Early, preliminary assessment of ethical implications*

➪ Many ethical challenges are not specific for PM!

Ethical implications of PM

Basic concept of PM: conceptually convincing

- If PM improves (*evidence-based*!) the effectiveness, safety and efficiency of health care delivery, promoting PM is an *ethical imperative*!

But: (potential) ambivalence of biomedical progress

- Assessment of ethical, legal, social & economic implications of PM
- Goal: ethically acceptable *development* and *application* of PM
- Cave: dominance of biological explanations!

Ethical Implications of PM: Overview

		Areas of personalized medicine		
		Research	*Application*	
			Prediction/Prevention	Therapy
Ethical issues	individual level	• Informed consent for add-on-studies • Informational self-determination • Confidentiality/ data protection	• Implication of predictive information about health risks? • Informational self-determination • Overemphasis of individual responsibility for health	• Higher risks due to insufficient testing (small groups of patients)? • (Confidentiality, data protection) • (Informational self-determination)
	societal level	• Allocation of research resources • Study design (patient relevant outcomes)	• Discrimination of „bad risks“ • (Access, distributive justice)	• Cost impact? => Access, distributive justice • (Discrimination of bad responders)

Modified according to Schleidgen 2011

Personalized Medicine & Justice: Overview

Distributive justice: 4 levels

Level	Area	Explanation
1	**Allocation** of research resources	Allocation of resources *into* personalized medicine (vs. alternative ways to promote health, prevent and treat diseases)
2		Allocation of resources *within* the field of personalized medicine
3	**Distribution** of PM products	Distribution of / access to personalized medicine
4	**Indirect consequences**	Discrimination/disadvantages due to diagnostic & prognostic information from personalized medicine

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Allocation of research resources (1)

Level 1: Allocation of resources *into* PM (vs. other alternatives)

- Central issue: high public and private investment in PM ⇨ right priorities?
  - Directed towards priority health needs of the population?
  - Higher health gain if resources are invested in other approaches?
  - Does it take into account existing inequalities in health status?

Policy options:

(1) Explicit priority setting in public funding for research
  - Health care needs in an ageing society (chronic diseases, multi-morbidity)
  - Priority for disadvantaged (sub-)populations
  - Potential for improving health status in population
  - Priority for common diseases?
  - Cost-effectiveness (efficiency) – anticipative assessment possible?

(2) Incentives for pharmaceutical companies to invest in areas with high priority

Allocation of research resources (2)

Level 2: Resource allocation *within* PM

- Investment in profitable areas ⇨ populations with rare (genetic) profile are neglected ⇨ „orphan populations“
- Neglect of vulnerable, already disadvantaged subpopulations
- Research with patient subgroups beyond PM neglected ⇨ higher risks through insufficiently tested interventions

Policy options

- Incentives for investments by pharmaceutical industry in „orphan populations“ (cf. current orphan drug regulation)
- More public research funding in (genetically) rare patient populations
- Challenge: increasing number of „orphan drugs“ ⇨ increasing public spending necessary ⇨ limits? priorities?

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Distribution of personalized medicine (3)

Justice requires: General & equal access to personalized medicine

Central question: *Will health care become more or less expensive with PM?*

Optimistic scenario: *Cost savings* through targeted therapies with a higher effectiveness and less side effects

Pessimistic scenario: *cost increase* due to additional (biomarker) diagnostic, high costs for R&D and production of PM for small populations ("niche busters")

Cost increase ⇨ (potentially) limited access for less affluent patients with less comprehensive insurance coverage
⇨ Creation of new & aggravation of existing inequalities (on a national and global scale!)

Distribution of personalized medicine (3)

Cost-effectiveness depends on several factors:

- Size of target population
- Number & cost of biomarker tests (i.e. test strategy)
- Likelihood of modified treatment decision due to diagnostic
- Cost impact of modified treatment decision

➪ Cost-effectiveness varies considerably! (Wong et al. 2010)

➪ Individual assessment of C/E-ration for each PM intervention

➪ *Shape* the cost-effectiveness of PM!

➪ HNPCC-screening: between 20.000€ and 1.500.000€/LYS depending on test strategy! (Mayer & Rogowski 2011)

Challenge (e.g. in oncology):

- Small incremental benefit ⇨ bad cost-effectiveness (HER-2 & Trastuzumab: $125.000/QALY [Elkin et al. 2004])

➪ Does the (small) additional benefit (at the end of life) justify the high costs?

Distribution of personalized medicine (3)

Cost-benefit-assessment requires valid *benefit* assessment!

At the time of licensing of the drug: benefit under routine conditions difficult to assess

- Studies for licensing: usually assess efficacy under ideal conditions
- Selected, not representative samples
- Surrogate endpoints instead of patient relevant endpoints (⇨ overall survival, quality of life)
- No head-to-head comparison with standard treatment
- Incomplete data transparency (reporting & publication bias)

⇨ Requirements for a needs oriented and fair allocation & distribution are often not met!

Distribution of personalized medicine (3)

Policy options

(1) First: Improve benefit assessment

- Independent, publicly financed clinical studies after licensing of the drug (patient relevant outcomes)
- (Initially) coverage only in clinical studies („coverage with evidence development“)
- (Germany: benefit assessment according to AMNOG too early!)

(2) Then: Cost-benefit assessment (CEA/CUA)

- Price negotiations with pharmaceutical industry
- Limited of coverage of interventions with bad incremental C/E-ratio
- Goal: unlimited access to *real innovations* for all patients, exclusion of „pseudo innovations“

Problem in Germany (& other countries): so far no open socio-political discourse on setting limits fairly in the hc system!

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Indirect consequences (level 4)

Discrimination of patient subgroups through *secondary* information of PM about

- risk of disease, prognosis, treatment effectiveness
- Categorization: „good responder“ ⇔ „non-responder“, „difficult to treat“

Fairness implications:

- ➪ Restricted access to health care interventions
- ➪ Restricted access to health insurances or higher premiums
- ➪ Disadvantages in other areas (e.g. employment)
- ➪ Stigmatization of subpopulations

Policy options

- ➪ Restrictive regulation of access to sensitive (genetic) information (e.g. only physician & patient, patient controls access)
- ➪ Informed consent for testing: Information about (indirect) risks

Conclusion

Personalized medicine has (potentially) ethical implications

➪ most are not specific for PM

➪ depend on application of individualized strategies

Individualized prediction & prevention: mainly challenges on the individual level (excess diagnostic information!)

Individualized treatment: mainly challenges on societal level

- Allocation of research resources into/within PM
- Distribution of PM interventions (cost-effectiveness!)

No general rejection of PM, but

(1) „Monitoring“ of ethical implications

(2) Implement policies to ensure ethically acceptable development and application of PM

➪ *Shape* the development in the field of PM!

Finally...

I would like to thank

- *your* for your attention
- *my colleagues* in the BMBF-collaborative research project for their input
  - Sebastian Schleidgen (ethics)
  - Elisabeth Meyer/Wolf Rogowski (economics)
  - Simone von Hardenberg/Nikola Wilman (law)

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