IMI ADAPT SMART
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Glossary of definitions of common terms

This glossary provides working definitions for common terms relevant for the ADAPT SMART consortium. The glossary is based on the input from members of the ADAPT SMART consortium representing different stakeholder groups. The definitions are based on relevant legislation or literature sources and written in the context of the ADAPT SMART project; where applicable, an EU perspective was chosen. Some definitions have been created without any direct reference source and these are shown as 'ADAPT SMART'.

Nr.	Term	Definition	Reference(s)
1.	Accelerated assessment (in EU regulatory framework)/	Rapid assessment of medicines in the centralised procedure that are of major interest for public health, especially ones that are therapeutic innovations.	EMA Glossary 2016a
2.	Adaptive clinical trial	A clinical trial that includes a prospectively planned opportunity for modification of one or more specified aspects of the clinical trial design and hypotheses based on analysis of data (usually interim data) from subjects in the clinical trial *See also 'Clinical trial'*	Based on FDA 2010
3.	Adaptive licensing (AL) Also: - Life cycle approach - Progressive licensing - Staggered approval	A prospectively planned, flexible approach to marketing authorisation of medicinal products. Through iterative phases of evidence gathering to reduce uncertainties followed by regulatory evaluation and license adaptation, AL seeks to maximize the positive impact of new medicinal products on public health by balancing timely access for patients with the need to assess and to provide adequate evolving information on benefits and harms so that better-informed patients-care decisions can be made.	H-G Eichler et al. 2012

Nr.	Term	Definition	Reference(s)
4.	Adaptive pathways	A prospective planned approach of development involving all stakeholders to support patient access to medicinal products answering an unmet medical need. It foresees an initial marketing authorisation and reimbursement of a medicinal product in a well-defined patient subgroup and subsequent widening of the indication to a larger patient population based on additional evidence gathered and/or a conditional marketing authorisation and conditional reimbursement where initial data are confirmed through the collection of post-authorisation data on the medicinal product's use. *See also 'Adaptive licensing'*	H-G Eichler et al. 2012
5.	Administrative claims data	Data that arises from a person's use of the healthcare system (and reimbursement of healthcare providers for that care).	GetReal 2016
6.	Advanced therapy medicinal product/ medicines (ATMPs)	A medicine for human use that is based on genes, cells or tissue engineering.	EMA Glossary 2016a
7.	Adverse event	Any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment.	European Commission 2001a
8.	Adverse reaction	1. Adverse reaction: A response to a medicinal product that is noxious and unintended that are related to any dose. 2. Serious adverse reaction: An adverse reaction which results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect. 3. Unexpected adverse reaction: An adverse reaction, the nature, severity or outcome of which is not consistent with the summary of product characteristics.	European Commission 2001b
9.	Appropriate use	Appropriate use refers to the situation in which medicinal products are prescribed, dispensed and administered in accordance with the SmPC.	ADAPT SMART
10.	Approval/ Authorisation under exceptional circumstances	A type of marketing authorisation granted to medicines where the applicant is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the condition to be treated is rare or because collection of full information is not possible or is unethical.	EMA Glossary 2016c
11.	Basket trial	Trial that studies a single targeted therapy in the context of multiple diseases or disease subtypes.	Woodcock et al. 2017
12.	Bayesian methods	Approaches to data analysis that provide a posterior probability distribution for some parameter (e.g. treatment effect), derived from the observed data and a prior probability distribution for the parameter. The posterior distribution is then used as the basis for statistical inference.	ICH 1998
13.	Benefit	The positive therapeutic effects of a medicinal product.	ADAPT SMART

Nr.	Term	Definition	Reference(s)
14.	Benefit-risk balance	An evaluation of the positive therapeutic effects of the medicinal product in relation to the risks.	European Commission 2001b
15.	Big data	Diverse datasets the size of which is beyond traditional evidence datasets. The size of the datasets is beyond the ability of typical database software tools to capture, store, manage, and analyse. Please note: This definition is intentionally subjective and incorporates a moving definition of how big a dataset needs to be in order to be considered big data.	Based on McKinsey & Company 2011
16.	Biomarkers	Any substance, structure, or process that can be measured in the body or its products and influence or predict the incidence of outcome or disease.	International Programme on Chemical Safety 2001
17.	Clinical endpoint/ outcome	An aspect of a subject's clinical or health status that is measured to assess the benefit or harm of an intervention. A clinical endpoint describes a valid measure of clinical benefit due to intervention: the impact of the intervention on how a subject feels, functions and survives.	Based on EUnetHTA 2013
18.	Clinical Guideline/ Medical Guideline	A document produced with the intention to guide decisions and inform criteria with regards to disease prevention, disease diagnosis, disease management, and treatment in the routine clinical setting.	GetReal 2016
19.	Clinical study	Any investigation in relation to humans intended: (a) to discover or verify the clinical, pharmacological or other pharmacodynamic effects of one or more medicinal products; (b) to identify any adverse reactions to one or more medicinal products; or (c) to study the absorption, distribution, metabolism and excretion of one or more medicinal products; with the objective of ascertaining the safety and/or efficacy of those medicinal products;	European Commission 2014
20.	Clinical trial	A clinical study which fulfils any of the following conditions: (a) the assignment of the subject to a particular therapeutic strategy is decided in advance and does not fall within normal clinical practice of the Member State concerned; (b) the decision to prescribe the investigational medicinal products is taken together with the decision to include the subject in the clinical study; or (c) diagnostic or monitoring procedures in addition to normal clinical practice are applied to the subjects.	European Commission 2014
21.	Cohort study	A study in which a group of subjects, sampled from a certain source population, are classified according to their exposure or determinant status and followed over time to ascertain the occurrence of a certain outcome.	GetReal 2016
22.	Companion diagnostic	A diagnostic test that provides information that is essential for the safe and effective use of a corresponding medicinal product. The test helps a health care professional determine whether a particular therapeutic product's benefits to patients will outweigh any potential serious side effects or risks.	ADAPT SMART
23.	Comparative effectiveness research	The conduct and/or synthesis of research comparing different benefits and harms of alternative interventions and strategies to prevent, diagnose, treat, and monitor health conditions in routine clinical practice (i.e. the real world setting). Comparative effectiveness research includes both primary data collection and secondary analyses (such as systematic literature reviews, meta-analyses and economic evaluations).	GetReal 2016

Nr.	Term	Definition	Reference(s)
24.	Comparator	Reference intervention to which safety, efficacy and/or effectiveness of a health intervention (e.g. pharmaceutical product) are compared. In the case of clinical trials for pharmaceutical products, comparators can comprise a placebo treatment (placebo-control trials), available standard of care, and/or a licensed medication (active-control trial).	GetReal 2016
25.	Compassionate use	Making a medicinal product available for compassionate reasons to a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who cannot be treated satisfactorily by an authorised medicinal product (the medicinal product concerned must either be subject of an application for a central marketing authorisation or must be undergoing clinical trials).	European Commission 2004
26.	Competent Authority	A regulatory authority in the European Union	Based on EMA Glossary 2016d
27.	Conditional marketing authorisation	A marketing authorization within the European Union with annual review, and which applies in specific cases: (a) Seriously debilitating or life-threatening diseases; (b) Emergency threats determined by the WHO, or the EU Commission; (c) Orphan medicinal products). The authorisation may be granted although comprehensive clinical data have not been supplied because it answers an unmet medical need. The available data must indicate that the medicine's benefits outweigh its risks and the applicant should be in a position to provide the comprehensive clinical data in the future.	Based on European Commission 2006 and EMA Glossary 2016b
28.	Conditional reimbursement	A recommendation to fund the use of a medicinal product, which includes a requirement to collect additional information to inform subsequent definitive decisions on coverage.	Based on Chalkidou et al. 2017
29.	Confounding bias	Systematic error that occurs when the estimate of a measure of association between exposure (e.g. healthcare intervention) and outcome (e.g. health status) is distorted by the effect of one or several extraneous variables (confounding factor(s)) that are independently related to the exposure and/or outcome.	GetReal 2016
30.	Controlled distribution	A controlled distribution system refers to a set of measures implemented to ensure that all stages of the distribution chain of a medicinal product are tracked up to the prescription and pharmacy dispensing the product. For instance, these sort of measures could be considered to prevent misuse and abuse of medicines.	Based on Guideline on good pharmacovigilance practices (GVP) – Module XVI
31.	Cost effectiveness	The incremental monetary value of an intervention to its corresponding incremental effect on relevant health outcomes measures based upon an economic evaluation using an appropriate health economic model. The purpose of calculating cost-effectiveness is to structure evidence on clinical and economic outcomes in a form that can help to inform decisions about clinical practices and health-care resource allocations *See also 'Health Economic Model'*	Based on M. Drummond and McGuire 2001 and Weinstein et al. 2003

Nr.	Term	Definition	Reference(s)
32.	Cost-effectiveness analysis	The economic evaluation of two (or more) alternative interventions where the costs and health effects of one intervention are compared to the costs and health effects of an alternative intervention (usually the standard of care)	Based on M. Drummond and McGuire 2001 and Weinstein et al. 2003
33.	Cost-utility analysis	An economic evaluation similar to cost-effectiveness analysis where the health effects of alternative interventions are conventionally determined by calculating corresponding quality-adjusted life-years (QALY's). Alternative methods for calculating utility exist and include Healthy Years Equivalent (HYE) and disability-adjusted life-year (DALY).	Based on M. Drummond and McGuire 2001 and Weinstein et al. 2003
34.	Coverage decisions	Decisions taken by health technology assessment bodies/healthcare payers/ insurers to determine allocation of resources with regards to which health interventions to reimburse, and the extent of reimbursement associated with the interventions covered by the payment package.	Based on GetReal 2014
35.	Coverage with evidence development	Makes coverage decisions conditional on the generation of further evidence through formal studies to support the value of the technology (such as a medicine). This allows a technology to be made available, usually for a defined period, after which the benefits of the technology are reviewed. *See also 'Managed entry agreement'*	Hutton, Trueman, and Henshall 2007
36.	Cross-design evidence synthesis	Comprises the pooling of, and analysis of, data from different studies. The studies from which data are combined can differ in relation to their design types, clinical setting, outcome measures, study interventions, study parameters, or patient/subject population. *See also 'Meta-analysis'*	Based on GetReal 2016
37.	Cross-over studies	Studies in which the subjects receive, in sequence, the experimental intervention (or the control intervention), then, after a specified time, (phase without intervention), the control intervention (or the experimental intervention).	Based on HTA Glossary 2006b
38.	Data exclusivity	The period of time from marketing authorisation of a medicinal product during which a company cannot cross-refer to the data from a registered product in support of another marketing authorisation.	ADAPT-SMART
39.	Direct treatment comparison	The comparison of the relative effect(s) of several interventions for a particular therapeutic indication in a trial setting. The basis for comparison can vary (e.g. clinical endpoints, adverse effect rates, or drug adherence rates) and the trial type may vary (e.g. randomised controlled clinical trial, pragmatic clinical trial or observational study). *See also 'Comparator' and 'Comparative effectiveness research'*	Based on GetReal 2016

Nr.	Term	Definition	Reference(s)
40.	Disability-adjusted life-year (DALYs).	The sum of years of life lost to premature mortality and the equivalent years of life lived with disability. DALYs provide an alternative approach to QALYs for the calculation of utilities in cost-utility analysis. *See also 'Quality-adjusted life-year' and 'Cost-utility analysis'*	Edejer et al. 2003
41.	Drug utilisation	This is defined by the World Health Organisation as 'the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences' (WHO 1977). This broad definition contains 2 aspects: the process of drug utilisation, that is the movement of drugs along the drug chain in society, and how drug utilisation relates to the effects of drug use.	GetReal 2016
42.	Drug utilisation studies	Research designed to investigate drug utilisation. Drug utilisation studies can be either retrospective or prospective, qualitative or quantitative. *See also 'Drug utilisation'*	GetReal 2016
43.	Early access programs	Programs that enable physicians and patients in the European Union to access medicinal products that are not yet authorized by the European Commission or National Competent Authorities (NCA). *See also* '*Compassionate use'*	Based on Urbinati, Masetti, and Toumi 2012
44.	Effectiveness	The extent to which an intervention does more good than harm when provided under the usual circumstances of health care practice.	GetReal 2016
45.	Effectiveness study	Measuring the effects of the healthcare intervention when prescribed to the subject under routine clinical practice and usual prescription conditions.	ADAPT SMART
46.	Efficacy	This refers to the benefits (e.g. to health outcomes) a health intervention produces under controlled conditions.	ADAPT SMART
47.	Efficacy study	Clinical study aimed at demonstrating the efficacy of a healthcare intervention under controlled conditions.	Based on Luce et al. 2010
48.	Efficacy-effectiveness gap	The observed discrepancy between effects of a health intervention in routine clinical practice as compared with the effects demonstrated in controlled conditions.	GetReal 2016
49.	Electronic health record/electronic medical record (EHR/EMR)	An electronic record of health-related information on an individual that can be created, gathered, managed, and consulted by authorized clinicians and other healthcare professionals. Patient/subject health-related information may include all of the key administrative clinical data relevant to that person's care under a particular provider, including demographics, progress notes, problems, medications, vital signs, past medical history, immunizations, laboratory data and radiology reports.	Based on GetReal 2016

Nr.	Term	Definition	Reference(s)
50.	Electronic healthcare data	Analytic data that is "an organized set of [healthcare] data or collection of files available by computer through electronic format which can be used for the conduct of [safety] studies". It is derived from a raw electronic healthcare database. Electronic healthcare data may include administrative claims data and electronic medical record (EMR) data. *See also 'Electronic health/medical record (I/EMR)' and 'Administrative claims data'*	Based on GetReal 2016
51.	Evidence versus access conundrum	A delicate trade-off between encouraging rapid patient access to promising therapies on the one hand, while on the other hand ensuring that patients and their regulatory and physician proxies possess adequate information on the therapy's benefits and risks at the time of marketing authorization.	Based on H-G Eichler et al. 2015
52.	Explanatory trials	Trials expected to have a high degree of internal validity and to be tightly designed to reflect the intended indication and treatment regimen, so that the errors and biases will influence the results as little as possible. This will control for sources of bias (systematic errors) by means of randomisation, blinding, and allocation concealment and will have a clearly defined participant population.	EMA 2015
53.	External validity/ Generalizability/ Applicability	Whether the results of a study, based on a sample of patients, when generalized beyond the study population, will be representative of results in a broader patient population.	Based on GetReal 2016
54.	Facilitated Regulatory Pathways (FRPs)	Regulatory pathways designed to accelerate submission, review and approval of medicines where there is an unmet medical need by providing alternatives to standard regulatory review routes. *See also 'Accelerated assessment/accelerated approval, 'Adaptive licensing', and 'Adaptive pathways'*	Liberti et al. 2015
55.	Flexible (adaptive) pricing scheme	Flexible pricing is where a scheme member can apply for an increase or decrease to a medicine's original list price in light of new evidence for use being developed.	Based on NHS 2014
56.	Hazard	A source of potential harm from past, current, or future exposures	ATSDR Glossary 2016
57.	Health care systems	The infrastructure and processes to support the health of a population.	Based on WHO 2000 and WHO 2016a
58.	Health Economic Model	A logical mathematical framework demonstrating the quantitative relationship between a defined set of variables (e.g. cost, effectiveness, net benefit) based upon an explicit set of parameters and assumptions. The purpose of modelling is to structure evidence on clinical and economic outcomes in a form that can help to inform decisions about clinical practices and health-care resource allocations.	GetReal 2016
59.	Health survey	Questionnaires designed to collect descriptions of health status and well-being, healthcare utilization, treatment patterns, and health-care expenditures from patients, providers, or individuals in the general population.	GetReal 2016

Nr.	Term	Definition	Reference(s)
60.	Health Technology Assessment (HTA)	The systematic evaluation of the properties and effects of a health technology, addressing the direct intended effects of this technology, as well as its indirect unintended consequences, and aimed mainly at informing decision-making regarding health technologies.	GetReal 2016
61.	Health-Related Quality of Life (HRQoL)	A patient-reported outcome that quantifies the impact of a medicine on a patient's quality of life by means of a validated instrument. Instruments can be either disease-specific or generic.	ADAPT SMART
62.	Healthy Years Equivalent (HYE)	An alternative approach to the QALY for the calculation of utilities in cost-utility analysis. Calculation of HYE differs from QALYs in two respects; firstly, preferences are measured over the entire path of health states through which an individual would theoretically pass and secondly, preferences are measured using a two-stage standard gamble measurement procedure. *See also 'Quality-adjusted life-year' and 'Cost-utlity analysis'*	Based on M. F. Drummond et al. 2005
63.	Historical control	A control group composed of subjects that have been observed previously to the present study.	Based on HTA Glossary 2006c
64.	Incremental Cost-Effectiveness Ratio (ICER)	The results of a cost-effectiveness analysis or cost-utility analysis are usually expressed by an ICER. The ICER expresses the incremental costs divided by the incremental effects of a new intervention against the standard of care (formula: ICER = Δcosts / Δeffects).	ADAPT SMART
65.	Indication	A clinical symptom, disease, risk factor or circumstance for which the use of a particular intervention would be appropriate, as recommended in a clinical practice guideline or protocol of care, or by a regulatory body or other authoritative source.	HTA Glossary 2006d
66.	Indirect treatment comparisons	The comparison of several interventions for a particular therapeutic indication (ideally versus the same control) in the absence of a study that directly compares the interventions in question.	Based on GetReal 2016
67.	Individual patient data (IPD) / Patient-level data	Raw data for subjects included in a study as opposed to aggregate data (summary data for the comparison groups in each study).	GetReal 2016
68.	Information bias	A flaw in measuring exposure, covariate, or outcome variables that results in different quality (accuracy) of information between comparison groups. The occurrence of information biases may not be independent of the occurrence of selection biases.	GetReal 2016
69.	Internal validity	The extent to which study attributes (e.g. study design) keep the possibility of systematic errors (i.e. biases) to a minimum.	GetReal 2016
70.	Interventional trial	*See 'Clinical trial'*	
71.	Licensing	*See 'Marketing authorisation'*	
72.	Life span (medicinal product)	All the stages of pre- and post-marketing until the product is withdrawn from the market.	ADAPT SMART

Nr.	Term	Definition	Reference(s)
73.	Live assets	Medicines in development either for initial approval or subsequent label extensions.	ADAPT SMART
74.	Longitudinal study	An observational study in which subjects are followed for the same variable(s) over a period of time.	Based on GetReal 2016
75.	Low intervention clinical trial	A clinical trial which fulfils all of the following conditions: (a) the investigational medicinal products, excluding placebos, are authorised; (b) according to the protocol of the clinical trial, (i)the investigational medicinal products are used in accordance with the terms of the marketing authorisation; or (ii) the use of the investigational medicinal products is evidence-based and supported by published scientific evidence on the safety and efficacy of those investigational medicinal products in any of the Member States concerned; and (c) the additional diagnostic or monitoring procedures do not pose more than minimal additional risk or burden to the safety of the subjects compared to normal clinical practice in any Member State concerned.	European Commission 2014
76.	Managed entry agreement	A formal arrangement between a company and a health technology assessment body/payer/provider that enables access to (coverage/reimbursement of) a health technology (such as a medicinal product) subject to specified conditions. These arrangements can use a variety of mechanisms to address uncertainty about the performance of the technology, or to manage the adoption of the technology in order to manage budget impact.	Based on Klemp, Frønsdal, and Facey 2011
77.	Managed introduction	A mechanism where governmental agencies and the marketing authorisation holder collaborate on the targeted introduction of new medicines, to achieve cost-effective and appropriate use for patients.	Based on Janusinfo
78.	Market-protection	The period of time during which a generic, hybrid or similar biological cannot be placed on the market even if it has already received marketing authorisation.	Frias 2013
79.	Marketing authorisation	A licence given by a regulatory authority to an applicant allowing for the marketing of a specific product within the jurisdiction of the regulatory agency. The decision for granting a marketing authorisation is based primarily on the quality, safety and efficacy of the new medicinal product and is based on the evidence of a positive benefit/risk ratio at the time of approval, i.e. the expected benefits outweigh the anticipated risks in a defined population, at a defined dosing and dose regimen, with defined conditions of use. *See also 'licensing'*	ADAPT SMART
80.	Medicinal product	Any substance or combination of substances which may be administered to human beings and are presented as having properties for treating or preventing disease and/or restoring, correcting or modifying physiological functions and/or making a medical diagnosis.	Based on European Commission 2001b

Nr.	Term	Definition	Reference(s)
81.	Medicines Adaptive Pathways to Patients (MAPP)	An EU initiative that seeks to provide timely access to medicines with potential to address significant unmet medical needs in a sustainable way. The MAPPs' scope covers regulatory approval, health technology assessment (HTA), pricing, reimbursement, and health care delivery. The general principle is that approval and reimbursement decisions are made using a framework which supports the launch of the therapy based on initial evidence. Additional data generated post-launch supports progressive reduction of uncertainty about benefits and risks and may lead to adjustments in utilisation and price in response to the emerging information. *See also 'Adaptive pathways' and 'Adaptive licensing'*	Based on Lucas 2014 and H-G Eichler et al. 2012
82.	Meta-analysis	The statistical combination of quantitative evidence from multiple studies to address common research questions where the analysis preserves the within-study comparisons.	Based on GetReal 2016
83.	Network meta-analysis	An extension of meta-analysis, allowing for the comparison of the relative effects of multiple treatments, either with or without the presence of a common comparator against which all interventions are studied. Network meta-analysis methods take into account direct and indirect treatment comparisons and pairwise meta-analysis. *See also 'Direct treatment comparison' and 'Indirect treatment comparison'*	GetReal 2016
84.	Non-interventional study	A study where the investigator does not interfere with choice of the prescribed health intervention i.e. interventions are prescribed in the usual manner in accordance with the terms of the marketing authorisation. The assignment of the subject to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice and the administration of the intervention is clearly separated from the decision to include the subject in the study. No additional diagnostic or monitoring procedures are applied to the subjects and epidemiological methods are used for the analysis of collected data.	Based on European Commission 2001a and GetReal 2014
85.	Normal clinical practice	The treatment regime typically followed to treat, prevent, or diagnose a disease or a disorder.	European Commission 2014
86.	Observational data	Data that are obtained from observing the use of a medicinal product in clinical practice.	ADAPT SMART
87.	Observational study	An observational study is a study in which a researcher simply observes behaviour in a systematic manner without influencing or interfering with the behaviour.	Psychology & Society 2014
88.	Off label	Situations where a medicinal product is intentionally used for a medical purpose not in accordance with the authorised product information.	Guideline on good pharmacovigilance practices (GVP) – Module VI
89.	Open utilization	Physicians have near-complete freedom of prescribing drugs off- label, without evidence generation.	H-G Eichler et al. 2015

Nr.	Term	Definition	Reference(s)
90.	Orphan designation (EU)	A status assigned to a medicinal product in development intended for a rare condition. The medicine should fulfil certain criteria for designation as an orphan medicinal product so that it can benefit from incentives such as protection from competition once on the market.	Based on EMA Glossary 2016e
91.	Orphan medicinal product	A medicine for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition that is rare (affecting not more than five in 10,000 people in the European Union) or where the medicine is unlikely to generate sufficient profit to justify research and development costs.	EMA Glossary 2016f
92.	Outcomes-based arrangements / contracts	An agreement which defines how to demonstrate product value, while mitigating financial risk and considering real-world factors, such as medication adherence or complex comorbidities that may influence effectiveness of a treatment. The performance of the product is measured in a defined patient cohort over a finite period of time using a key outcome.	Based on Nazareth et al. 2016
93.	Outcomes study	A field of inquiry that focuses on health problems or diseases and that is essentially aimed at evaluating the care delivered by multidisciplinary teams in general, real-world settings.	HTA Glossary 2006e
94.	Patient access	The degree to which a patient or group is able to obtain care or services, taking into account the health system's financial and organisational constraints.	HTA Glossary 2006a
95.	Patient access pathway	The process from clinical development through marketing authorization, payer coverage and reimbursement processes to health care system adoption and use in patients.	ADAPT SMART
96.	Patient awareness	The degree to which a patient or group of patients have knowledge about treatment options	ADAPT SMART
97.	Patient involvement	Patients' role in activities or decisions that will have consequences for the patient community, because of their specific knowledge and relevant experience as patients.	EUPATI 2013
98.	Patient preferences	The aspects of a treatment which a patient or group of patients indicate as relevant for choosing between treatment options.	ADAPT SMART
99.	Patient-Reported Outcome (PRO)	A measurement based on a report that comes directly from the patient (i.e., study subject) or a caregiver about the status of the patient's health condition, without amendment or interpretation of the patient's response by a clinician or anyone else.	Based on GetReal 2016
100.	Patient relevant outcome	A measure of how a patient will respond to a treatment using factors, which patients consider to be important e.g. quality of life.	Based on Pavlovic et al. 2014
101.	Patient Support Programme (PSP)	A patient support programme is a set of activities organized by a marketing authorisation holder involving direct interaction of healthcare professionals with patients, with the purpose of providing healthcare services to patients related to the use of medicines (especially in chronic disease states). The underlying objective may be for example to help patients better manage their disease and their medication regimen, reduce the burden of treatment, improve medication adherence, collect information, and reduce complications and costs.	Based on Shillington et al. 2016

Nr.	Term	Definition	Reference(s)
102.	Patient values	The considerations that are important to an individual patient or group of patients.	ADAPT SMART
103.	Payers	Regional or national organisations responsible for managing healthcare budgets and/or responsible for providing payment/reimbursement for treatments/medical care.	ADAPT SMART
104.	Pay-for-performance model	A payment model that typically involves only paying for patients that experience treatment benefit or not paying for patients who experience early treatment failure.	ADAPT SMART
105.	Personalised medicine	A medicine that is targeted to individual patients or stratified population of patients with specific characteristics. Personalised medicine can also be interpreted more narrowly to mean targeted treatment according to genetic variations only or to mean a unique treatment for the individual patient rather than groups of patients. *See also 'Stratified medicine' and 'Precision medicine'*	Based on EMA Glossary 2016g
106.	Pharmacotherapeutic gaps	Gaps where treatments either do not exist or are inadequate, or where existing treatments are likely to become ineffective in the future.	Kaplan et al. 2013
107.	Pharmacometrics	An emerging science defined as the science that quantifies drug, disease and trial information to aid efficient drug development and/or regulatory decisions.	Based on FDA 2015
108.	Pharmacovigilance	Science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem.	EMA Glossary 2016h
109.	Phase 1 trials	A first in human clinical trial usually involving healthy volunteers to investigate a drug's safety, safe dosage range, pharmacokinetic characteristics (absorption, distribution, metabolic activity, excretion) and duration of activity.	Based on HTA Glossary 2006f
110.	Phase 2 (2a, 2b) trials	Clinical trials to further explore dosage, efficacy and safety in subjects.	ADAPT SMART
111.	Phase 3 (3a, 3b) trials	Clinical trials to confirm dosage efficacy and safety in subjects.	ADAPT SMART
112.	Phase 4 trials	Studies performed in a post-marketing setting which are designed to monitor effectiveness and safety of the approved intervention in the general population and also potentially in a 'real-world' setting.	Based on GetReal 2016
113.	Planned access	Prospective planning by all stakeholders together on how a health technology (such as a medicinal product) can be developed and taken into the market to enable appropriate utilisation.	ADAPT SMART
114.	Platform trial	Trial that studies multiple targeted therapies in the context of a single disease in a perpetual manner, with therapies allowed to enter or leave the platform on the basis of a decision algorithm.	Woodcock et al. 2017
115.	Post-authorisation	The period that commences immediately after marketing authorization of a medicinal product is granted.	ADAPT SMART

Nr.	Term	Definition	Reference(s)
116.	Post-Authorisation Efficacy Studies (PAES)	Studies conducted within the authorised therapeutic indication to complement available efficacy data in the light of well-reasoned scientific uncertainties on aspects of the evidence of benefits that should be, or can only be, addressed post-authorisation. A PAES may be initiated, managed or financed by a marketing authorisation holder (MAH) voluntarily, or pursuant to an obligation imposed by a competent authority.	EMA 2015
117.	Post-Authorisation Safety Studies (PASS)	Any study relating to an authorised medicinal product conducted with the aim of identifying, characterising or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures.	European Commission 2001b
118.	Post-marketing	The period after launch of a product in the market.	ADAPT SMART
119.	Pragmatic trial	Pragmatic trials examine interventions under circumstances that approach real-world practice, with more heterogeneous patient populations, possibly less-standardised treatment protocols, and delivery in routine clinical settings as opposed to a research environment. Minimal restrictions may be placed on modifying dose, dosing regimens, co-therapies or co-morbidities or treatment switching.	EMA 2015
120.	Pre-authorisation	The period prior to the granting of the marketing authorisation ("approval") / license for a specific pharmaceutical/ medical device product. *See also 'Pre-authorisation drug development'*	GetReal 2016
121.	Pre-authorisation drug development	Research and development performed in order to discover new active substances and subsequently demonstrate safety and efficacy of a new medicinal product in order to gain marketing authorisation.	Based on GetReal 2016
122.	Precision medicine	The ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease, in the biology and/or prognosis of those diseases they may develop, or in their response to a specific treatment in order to better match patients with therapies. *See also 'Stratified medicine'*	Based on PCAST 2008
123.	Predictive modelling	The activity of developing, validating or adapting models which relate a dependent variable with a set of independent variables in a manner similar to multiple regression analysis. For the purposes of the IMI ADAPT SMART project, this predictive modelling is designed to predict the (relative) effectiveness of a medical intervention from available clinical and trial based efficacy/effectiveness data.	Based on GetReal 2016
124.	Prescribing controls	Healthcare systems restrictions on the patient population for which the medicinal product can be prescribed.	ADAPT SMART
125.	Priority medicines	Those medicines, which are needed to meet the priority health care needs of the population.	Based on Kaplan et al. 2013

Nr.	Term	Definition	Reference(s)
126.	Promising therapy	Medicinal product that is likely to offer benefit or provide a significant advantage over and above existing treatment options.	Based on MHRA 2014
127.	Protocol assistance	A special form of scientific advice available for companies developing designated orphan medicines. *See also 'Orphan designation'*	EMA 2009
128.	Quality – Adjusted Life Years (QALYS)	A health outcome measure that captures both the impact of an intervention on a patient's health-related quality of life (i.e. utility) as well as the patient's remaining life expectancy (i.e. mortality). Utility measures conventionally range from 0 (death) to 1 (perfect health). The QALY is calculated by multiplying the utility by the time spent in the given health state. One QALY equals one year lived in full health. See also 'Cost-utility analysis'	Based on M. F. Drummond et al. 2005
129.	Randomisation	The process of allocating clinical trial participants to treatment or control groups, using chance to determine the assignments. It aims to ensure the initial comparability of participants between the treatment groups, equalizing the distribution of confounding factors, whether they are known or unknown, in order to be able to attribute to the treatment any differences observed between groups.	ADAPT SMART
130.	Randomised Controlled Trial (RCT)	Clinical trial designed to test the efficacy and/or safety of an intervention within a sample of selected subjects. These are subjected to predefined inclusion and exclusion criteria, and randomly assigned to two or more groups (at least one treatment and one control group).	Based on GetReal 2016
131.	Rational use	Rational use of medicines: requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community.	Ministry of Health, Welfare and Sport, The Netherlands 2012 and WHO 2016b
132.	Real World Data (RWD)	An umbrella term for data regarding the effects of health interventions (e.g. benefit, risk, resource use, etc.) that are collected both prospectively and retrospectively from observations of routine clinical practice. RWD can be obtained from many sources including patient registries, electronic medical records, and observational studies.	ADAPT SMART
133.	Real World Evidence (RWE)	Real World Evidence (RWE) is the evidence derived from the analysis and/or synthesis of real-world data (RWD) in support of safety, efficacy, effectiveness and/or clinical utility/cost-effectiveness.	Based on GetReal 2016
134.	Real World Study (RWS)	Studies that are conducted to evaluate a health intervention in clinical practice. *See also 'Real World Data (RWD)' and 'Real World Evidence (RWE)'*	ADAPT SMART
135.	Realised risk	The risk assessment using the additional insight gained from utilisation of the treatment in clinical practice.	ADAPT SMART

Nr.	Term	Definition	Reference(s)
136.	Regenerative medicines	Treatment to repair or replace tissue or organ function lost to age, disease, damage or congenital defects by creating living or functional tissues.	ADAPT SMART
137.	Registry	An organised system to collect uniform data on specified outcomes in a population defined by a particular disease, condition or exposure.	Based on EMA 2013
138.	Regulatory Authority/ Regulator (Relating to medicinal products)	A government body that carries out regulatory activities relating to medicinal products, including the processing of initial and existing marketing authorisations, the monitoring of side effects, inspections, quality control and the monitoring of post-marketing use of medicinal products.	Based on EMA Glossary 2014
139.	Regulatory pathway	The procedure and route used to assess the regulatory aspects of an application concerning a new treatment or diagnostic or new use for an existing treatment or diagnostic.	ADAPT SMART
140.	Regulatory science	A science that informs, facilitates and evaluates regulatory decision making, by producing standards, tools and structures to develop and evaluate evidence about the performance of medicinal products, and by producing evidence about the performance of the regulatory system.	Based on Leufkens and Eichler 2011
141.	Reimbursement	When the costs of healthcare consumption are (partly) paid by someone other than the patient receiving the treatment (usually either a national healthcare service or health insurer).	ADAPT SMART
142.	Relative effectiveness	The extent to which an intervention does more good than harm, compared to one or more intervention alternatives in achieving the desired results and when provided under the usual circumstances of health care practice.	Pharmaceutical Forum 2008 and H-G Eichler et al. 2010
143.	Risk	The combination of the probability of occurrence of harm and the severity of that harm.	ISO 2014
144.	Risk-sharing scheme	Agreement between a payer and a company regarding a health technology where the price level and/or revenue received is related to the future performance of the product based on outcome measures and/or financial impact.	Based on Towse and Garrison 2010
145.	Safe harbour environment	A forum in which discussions are confidential, non-binding and without implications for future discussions.	ADAPT SMART
146.	Scientific Advice	Guidance given by a regulatory authority and/or a HTA body and/or payer to a health technology developer on appropriate tests and studies to be performed during product development.	Based on GetReal 2016
147.	Stakeholder	An individual, organisation or initiative that participates in, is involved with, influences the outcomes of, or is impacted by the outcomes of, or implications of, a certain activity.	Based on GetReal 2016
148.	Standard of care	The current recognised benchmark diagnostic and/or treatment process in a specific healthcare setting.	ADAPT SMART
149.	Stratification	Grouping of patients/subjects by a characteristic e.g. biomarker, geographic location, or age.	ADAPT SMART

Nr.	Term	Definition	Reference(s)
150.	Stratified medicine	See 'Precision Medicine'	Based on Trusheim, Berndt, and Douglas 2007
151.	Sub-group analysis (relating to clinical trial)	Analysis conducted to assess whether, and how, observed endpoints in a study are sensitive to/ affected by characteristics attributable to a specific sub-group of the study population. Such characteristics can relate to, for example, age, gender, genotype, or patient/subject history.	GetReal 2016
152.	Subgroup (relating to clinical trial)	Any subset of the recruited patient population that fall into the same category (level) with regard to one or more descriptive factors. These factors and the categorisation of patients will usually be identifiable prior to randomisation based on both intrinsic and extrinsic factors (see ICH E5), including demographic characteristics (including genetic or other biomarkers), disease characteristics including severity or (pheno)type of disease and clinical considerations (e.g. use of concomitant medications, region or centre).	EMA 2014
153.	Surrogate endpoint	An indirect measurement of effect used in situations where direct measurement of clinical effect is not feasible or practical.	Based on GetReal 2016
154.	Sustainability	Ability to maintain or support long-term	ADAPT SMART
155.	Targeted population	The specific group to be studied /treated based upon one or more of their characteristics.	ADAPT SMART
156.	Timely access to treatment	Making a treatment available without undue delay	ADAPT SMART
157.	Treatment	An intervention e.g. using a medicinal product, a surgical procedure and/or medical device to improve health or well-being.	ADAPT SMART
158.	Treatment window of opportunity	The period during which individual patients diagnosed with a disease can potentially benefit from a novel treatment. *Note: Interpreted in context of ADAPT SMART to mean time of access to a novel treatment*.	Based on H-G Eichler et al. 2015
159.	Umbrella trial	Trial that studies multiple targeted therapies in the context of a single disease.	Woodcock et al. 2017
160.	Uncertainty	A situation where it is perceived by a stakeholder that additional information would be required to further qualify the benefits and risks and value of a medicinal product.	ADAPT SMART
161.	Unmet medical need	Life threatening or severely debilitating conditions for which no treatment or no satisfactory treatment exists. Note: This definition is used within the MAPPs context; there are other definitions, which are beyond the context of MAPPs (e.g. Conditional Marketing Authorisation Regulation (EC) 507/2006). The definition of unmet medical need is the subject of discussion and may evolve with time.	ADAPT SMART

References:

ATSDR Glossary. 2016. “Hazard.” Accessed January 22nd 2016. http://www.atsdr.cdc.gov/glossary.html#G-G-).

Chalkidou, K. *Conditional Reimbursement Based on Future Research*. https://www.ispor.org/news/articles/June08/CRB.asp.

Drummond, M.F., M.J. Sculpher, K. Claxton, G.L. Stoddart, and G.W. Torrance. 2005. *Methods for the Economic Evaluation of Health Care Programmes*. 3rd ed. Accessed February 18th 2016. ISBN 978-0-19-966587 (hbk.) 978-0-19-966588 (pbk.).

Drummond, M., and A. McGuire. 2001. *Economic Evaluation in Health Care: Merging Theory with Practice*. Oxford ; New York: Oxford University Press. Accessed February 10th 2016. ISBN 0192631772 (Hbk) 0192631764 (Pbk)

Edejer, T.T., R. Baltussen, T. Adam, R. Hutubessy, A. Acharya, D.B. Evans, and C.J.L. Murray, eds. 2003. *Making Choices in Health: WHO Guide to Cost-Effectiveness Analysis*. Geneva: World Health Organization. Accessed February 18th 2016. http://www.who.int/choice/publications/p_2003_generalised_cea.pdf

Eichler, H-G, L.G. Baird, R. Barker, B. Bloechl-Daum, F. Børlum-Kristensen, J. Brown, R. Chua, et al. 2015. “From Adaptive Licensing to Adaptive Pathways: Delivering a Flexible Life-Span Approach to Bring New Drugs to Patients.” *Clinical Pharmacology & Therapeutics* 97 (3): 234–46. Accessed February 10th 2016. doi:10.1002/cpt.59.

Eichler, H-G, K. Oye, L.G. Baird, E. Abadie, J. Brown, C.L. Drum, J. Ferguson, et al. 2012. “Adaptive Licensing: Taking the Next Step in the Evolution of Drug Approval.” *Clinical Pharmacology & Therapeutics* 91 (3): 426–37. Accessed February 10th 2016. doi:10.1038/clpt.2011.345.

Eichler, H-G, B. Bloechl-Daum, E. Abadie, D. Barnett, F. König, and S. Pearson. 2010. “Relative Efficacy of Drugs: An Emerging Issue between Regulatory Agencies and Third-Party Payers.” *Nature Reviews Drug Discovery* 9 (4): 277–91. Accessed February 10th 2016. doi:10.1038/nrd3079.

EMA. 2009. “Scientific Advice and Protocol Assistance.” Accessed February 10th 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000049.jsp&mid=WC0b01ac05800229b9.

———. 2013. “Guideline on Good Pharmacovigilance Practices (GVP) Module VIII – Post-Authorisation Safety Studies (Rev 1).” Accessed February 10th 2016. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500129137.pdf.

———. 2014. “Guideline on the Investigation of Subgroups in Confirmatory Clinical Trials.” Accessed February 10th 2016. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/02/WC500160523.pdf.

———. 2015. “Scientific Guidance on Post-Authorisation Efficacy Studies (draft).” Accessed February 10th 2016. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/11/WC500196379.pdf.

EMA Glossary. 2014. “Regulatory Authority.” Accessed February 10th 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=R.

———. 2016a. “Accelerated Assessment.” Accessed February 10th 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=A.

———. 2016b. “Conditional Approval.” Accessed January 19th 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=C.

———. 2016c. “Exceptional Circumstances.” Accessed February 12th 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=E.

———. 2016d. “National Competent Authority.” Accessed February 10th 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=N.

———. 2016e. “Orphan Designation.” Accessed February 12th 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=O.

———. 2016f. “Orphan Medicine.” Accessed February 10th 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=O.

———. 2016g. “Personalised Medicine.” Accessed February 10th 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=P.

———. 2016h. “Pharmacovigilance.” Accessed February 10th 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=P.

EUnetHTA. 2013. “Endpoints Used for Relative Effectiveness Assessment of Pharmaceuticals: Clinical Endpoints.” Accessed February 10th 2016. https://5026.fedimbo.belgium.be/sites/5026.fedimbo.belgium.be/files/Clinical%20endpoints.pdf.

EUPATI. 2013. “Patient Involvement.” Accessed February 10th 2016. http://www.patientsacademy.eu/index.php/en/2-uncategorised/83-glossary.

European Medicines Agency. *Guideline on good pharmacovigilance practices (GVP) - Module VI*.
———. *Guideline on good pharmacovigilance practices (GVP) – Module XVI*.

European Commission. 2001a. Directive 2001/20/EC, OJ L 121, 1.5.2001 p.34. Accessed February 10th 2016. http://ec.europa.eu/health/files/eudralex/vol-1/dir_2001_20/dir_2001_20_en.pdf

———. 2001b. Directive 2001/83/EC, OJ L 311, 28.11.2001, p.67. Accessed February 10th 2016. http://ec.europa.eu/health/files/eudralex/vol-1/dir_2001_83_consol_2012/dir_2001_83_cons_2012_en.pdf.

———. 2004. Regulation (EC) No 726/2004 OJ L 136 30.4.2004. Accessed February 10th 2016. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:136:0001:0033:en:PDF.

———. 2006. Commission Regulation (EC) No 507/2006 OJ L 92/6 30.3.2006. Accessed February 10th 2016. http://ec.europa.eu/health/files/eudralex/vol-1/reg_2006_507/reg_2006_507_en.pdf.

———. 2014. Regulation (EU) No 536/2014 OJ L158/1 27.5.2014. Accessed February 10th 2016. http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536&from=EN.

FDA. 2010. “Guidance for Industry: Adaptive Design Clinical Trials For Drugs and Biologics (Draft).” Accessed February 10th 2016. “http://www.fda.gov/downloads/Drugs/.../Guidances/ucm201790.pdf”

———. 2015. “Pharmacometrics at FDA.” Accessed February 10th 2016. http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm167032.htm.

Frias, Z. 2013. "Data exclusivity, market protection and paediatric rewards." Accessed April 14th 2016. http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2013/05/WC500143122.pdf

GetReal. 2014. “IMI-GetReal Glossary Work Package 1 (WP1) Deliverable D1.3.” Accessed February 10th 2016. http://www.imi-getreal.eu/Portals/1/Documents/Publications/D1.3%20GetReal%20Glossary.pdf & http://www.imi-getreal.eu/Portals/1/Documents/Public%20consultation/D1.3%20-%20GetReal%20glossary%20for%20consultation.docx.

Gliklich, R., N. Dreyer, and M. Leavy. 2014. *Registries for Evaluating Patient Outcomes: A User’s Guide. Two Volumes*. Accessed February 10th 2016.

http://effectivehealthcare.ahrq.gov/ehc/products/420/1897/registries-guide-3rd-edition-vol-1-140430.pdf.

HTA Glossary. 2006a. “Access.” Accessed February 10th 2016. http://htaglossary.net/access.

———. 2006b. “Crossover Design.” Accessed February 10th 2016. https://www.nlm.nih.gov/nichsr/hta101/ta101014.html.

———. 2006c. “Historical Control.” Accessed February 10th 2016. http://htaglossary.net/historical+control.

———. 2006e. “Indication.” Accessed February 10th 2016. http://htaglossary.net/indication.

———. 2006f. “Outcomes Research.” Accessed February 10th 2016. http://htaglossary.net/outcomes+research.

———. 2006g. “Phase I, II, II, IV Study.” Accessed February 10th 2016. http://htaglossary.net/Phase+I%2C+II%2C+III%2C+or+IV+study.

Hutton, J., P. Trueman, and C. Henshall. 2007. “Coverage with Evidence Development: An Examination of Conceptual and Policy Issues.” *International Journal of Technology Assessment in Health Care* 23 (04). Accessed February 10th 2016. doi:10.1017/S0266462307070651.

ICH. 1998. “Statistical Principles for Clinical Trials E9.” Accessed February 10th 2016. http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/Step4/E9_Guideline.pdf.

International Programme on Chemical Safety, ed. 2001. *Biomarkers in Risk Assessment: Validity and Validation*. Environmental Health Criteria 222. Geneva: World Health Organization. Accessed February 10th 2016. http://www.inchem.org/documents/ehc/ehc/ehc222.htm.

ISO. 2014. “ISO/IEC Guide 51:2014. Safety Aspects - Guidelines for Their Inclusion in Standards.” Accessed February 10th 2016. http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=53940.

Janusinfo. *Managed introduction – this is how it works*. http://www.janusinfo.se/Managed-introduction--this-is-how-it-works/.

Kaplan, W., V.J. Wirtz, A. Mantel-Teeuwisse, P. Stolk, B. Duthey, and R. Laing. 2013. WHO “Priority Medicines for Europe and the World 2013 Update.” Accessed February 10th 2016. http://www.who.int/medicines/areas/priority_medicines/MasterDocJune28_FINAL_Web.pdf.

Klemp, M., K.B. Frønsdal, and K. Facey. 2011. “What Principles Should Govern the Use of Managed Entry Agreements?” *International Journal of Technology Assessment in Health Care* 27 (01): 77–83. Accessed February 10th 2016. doi:10.1017/S0266462310001297.

Leufkens, H. and H-G Eichler. 2011. “Innovative Methods in Drug Regulatory Sciences.” *Drug Discovery Today: Technologies* 8 (1): e1–e2. Accessed February 10th 2016. doi:10.1016/j.ddtec.2011.07.001.

Liberti, L., P. Stolk, N. McAuslane, A. Somauroo, A.M. Breckenridge, and H. Leufkens. 2015. “Adaptive Licensing and Facilitated Regulatory Pathways: A Survey of Stakeholder Perceptions.” *Clinical Pharmacology & Therapeutics* 98 (5): 477–79. Accessed February 10th 2016. doi:10.1002/cpt.140.

Lucas, F. 2014. “Medicines Adaptive Pathways to Patients (MAPPs) – Opportunities and Challenges in Europe.” Accessed February 10th 2016. http://www.ispor.org/ValueOutcomesSpotlightResources/health-policy_MAPPS_Europe.PDF.

Luce, B.R., M. Drummond, B. Jönsson, P.J. Neumann, J.S. Schwartz, U. Siebert, and S.D. Sullivan. 2010. “EBM, HTA, and CER: Clearing the Confusion.” *The Milbank Quarterly* 88 (2): 256–76. Accessed February 10th 2016. doi:10.1111/j.1468-0009.2010.00598.x.

McKinsey & Company. 2011. “Big Data: The next frontier for Innovation, Competition, and Productivity.” Accessed February 10th 2016. http://www.mckinsey.com/insights/business_technology/big_data_the_next_frontier_for_innovation (download full report)

MHRA. 2014. “Apply for a Licence to Market a Medicine in the UK.” Accessed February 10th 2016. https://www.gov.uk/apply-for-a-licence-to-market-a-medicine-in-the-uk#l3.

Ministry of Health, Welfare and Sport, The Netherlands. 2012. “The Benefits of Responsible Use of Medicines: Setting Policies for Better and Cost-Effective Healthcare.” Accessed February 10th 2016. https://www.fip.org/centennial/files/static/REPORT_MINISTERS_SUMMIT_-_English_version_final.pdf.

Nazareth, T. “Outcomes-based arrangements in value-based care: An engagement framework”. https://www.ispor.org/research_pdfs/52/pdffiles/PHP214.pdf.

NHS. “The Pharmaceutical Price Regulation Scheme 2014”. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/621983/2014_PPRS_Scheme.pdf.

Pavlovic, Mira, Conor Teljeur, Beate Wieseler, Marianne Klemp, Irina Cleemput, en Mattias Neyt. 2014. “Endpoints For Relative Effectiveness Assessment (Rea) Of Pharmaceuticals”. *International Journal of Technology Assessment in Health Care* 30 (05): 508–13. doi:10.1017/S0266462314000592.

PCAST. 2008. “Priorities for Personalized Medicine.” Accessed February 17th 2016. https://www.whitehouse.gov/files/documents/ostp/PCAST/pcast_report_v2.pdf.

Pharmaceutical Forum. 2008. “Final Conclusions and Recommendations of the High Level Pharmaceutical Forum.” Accessed February 10th 2016. http://www.anm.ro/_/Final%20Conclusions%20and%20Recommendations%20of%20the%20High%20Level%20Pharmaceutical%20Forum.pdf.

Psychology & Society. 2014. “Observational Study.” Accessed February 10th 2016. http://www.psychologyandsociety.com/observationalstudy.html.

Shillington, Alicia, Arijit Ganjuli, en Jerry Clewell. 2016. “The Impact of Patient Support Programs on Adherence, Clinical, Humanistic, and Economic Patient Outcomes: A Targeted Systematic Review”. *Patient Preference and Adherence*, april, 711. doi:10.2147/PPA.S101175.

Towse, A., and L.P. Garrison. 2010. “Can’t Get No Satisfaction? Will Pay for Performance Help?: Toward an Economic Framework for Understanding Performance-Based Risk-Sharing Agreements for Innovative Medical Products.” *PharmacoEconomics* 28 (2): 93–102. Accessed February 10th 2016. doi:10.2165/11314080-000000000-00000.

Trusheim, M.R., E.R. Berndt, and F.L. Douglas. 2007. “Stratified Medicine: Strategic and Economic Implications of Combining Drugs and Clinical Biomarkers.” *Nature Reviews Drug Discovery* 6 (4): 287–93. Accessed February 10th 2016. doi:10.1038/nrd2251.

Urbinati, D., L. Masetti, and M. Toumi. 2012. “Early Access Programmes (EAPs): Review of European System.” Accessed February 10th 2016. http://www.creativ-ceutical.com/sites/default/files/Early%20Access%20Programmes_EU%20countries.pdf.

Weinstein, M.C., B. O’Brien, J. Hornberger, J. Jackson, M. Johannesson, C. McCabe, and B.R. Luce. 2003. “Principles of Good Practice for Decision Analytic Modeling in Health-Care Evaluation: Report of the ISPOR Task Force on Good Research Practices—Modeling Studies.” *Value in Health* 6 (1): 9–17. Accessed February 10th 2016. doi:10.1046/j.1524-4733.2003.00234.x.

WHO, ed. 2000. *The World Health Report 2000: Health Systems: Improving Performance*. Geneva: WHO. Accessed February 10th 2016. http://www.who.int/whr/2000/en/whr00_en.pdf?ua=1.

———. 2016a. “Health Systems Strengthening Glossary.” *WHO*. Accessed February 10. Accessed February 10th 2016. http://www.who.int/healthsystems/hss_glossary/en/index5.html.

———. 2016b. “Rational Use of Medicines.” *WHO*. Accessed February 10. Accessed February 10th 2016. http://www.who.int/medicines/areas/rational_use/en/.

Woodcock, Janet, en Lisa M. LaVange. 2017. “Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both”. Onder redactie van Jeffrey M. Drazen, David P. Harrington, John J.V. McMurray, James H. Ware, en Janet Woodcock. *New England Journal of Medicine* 377 (1): 62–70.

doi:10.1056/NEJMra1510062.