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Version: Accepted Version

Proceedings Paper:
Cornford, T and Lichtner, V (2014) Digital drugs: An anatomy of new medicines. In: Doolin, B, Lamprou, E, Mitev, N and McLeod, L, (eds.) Information Systems and Global Assemblages. (Re)Configuring Actors, Artefacts, Organizations. IFIP WG 8.2 Working Conference on Information Systems and Organizations 2014, 11-12 Dec 2014, Auckland, New Zealand. Springer Verlag, pp. 146-162. ISBN: 9783662457078. ISSN: 1868-4238. EISSN: 1868-422X.

https://doi.org/10.1007/978-3-662-45708-5_10

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Digital Drugs: An anatomy of new medicines[1]

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Abstract. Medicines are digitalized as aspects of their regulation and use are embodied in or draw from interlinked computerized systems and databases. This paper considers how this development changes the delivery of health care, the pharma industry, and regulatory and professional structures, as it reconfigures the material character of drugs themselves. It draws on the concept of assemblage in presenting a theory-based analysis that explores digital drugs' ontological status including how they embody benefit and value. The paper addresses three interconnected domains – that of use of drugs (practice), of research (epistemology) and of regulation (structures).

Keywords: Pharmaceutical Preparations; Individualized Medicine; Digital Drugs; Healthcare; Assemblage

1 Introduction

Anatomy: 1. The art of studying the different parts of any organized body, to discover their situation, structure, and economy; dissection. […] 4. The act of dividing anything, corporeal or intellectual, for the purpose of examining its parts; analysis; as, the anatomy of a discourse.
http://en.wiktionary.org/wiki/anatomy

Medicines[2] and the ways we use and regulate them are changing, transformed by digitalization [1]. This reconfiguration is associated with visions of scientific, ther-

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[1] A version of this paper was presented at IFIP Working Group 8.2 Information Systems and Organizations conference, *Information Systems and Global Assemblages: (Re)Configuring Actors, Artefacts, Organizations,* December 2014, Auckland, New Zealand. The conference version is published in Doolin, B., Lamprou, E., Mitev, N., McLeod, L. (Eds.) (2014) *Information Systems and Global Assemblages: (Re)Configuring Actors, Artefacts, Organizations*, IFIP WG 8.2 Working Conference, IS&O 2014, Auckland, New Zealand, December 11-12, 2014, Proceedings: IFIP Advances in Information and Communication Technology, Vol. 446. 2014, XII, 247 p. 15 illus.

apeutic, managerial and financial breakthroughs from 'better' medicines and in particular 'better' digitally mediated medicine use practices. Expectations include: help in meeting the needs of aging populations with multiple chronic diseases, the targeting of medicines to individuals (personalization) to significantly increase efficacy and reduce overall cost, and computerized clinical decision support that can reduce the burden of harm caused by adverse drug events (ADEs). The pharma industry too is reconfiguring as it faces increasing competition from 'generics', reductions in the pipeline of new medicines entering the market and the 'patent cliff' off which large pharma companies fear to fall [2, 3]. Such pressures spur changes in how current drugs are marketed, distributed and paid for [4]. Pharmaceutical business models are realigned to build new relations between patients, health care institutions and the pharma industry, with drug products enmeshed in or recast as a set of services, and with payment (pricing/reimbursement) shifting from the 'product' to outcomes.

The digitalization of medicines is reflected in a number of overlapping areas of contemporary research and development including *electronic prescribing, stratified medicine*, *personalized medicine*, *smart drug platforms*, *medical profiling*, *pharmacovigilance, value based pricing* and *pharmacogenomic*s (Table 1). The specifics of the 'breakthrough' vision vary, as do the digital mechanisms and resources that are imagined or deployed, but taken overall these initiatives seem to offer new possibilities for therapeutic improvement and innovation through digitally mediated ways of using drugs. We believe they also foreshadow multiple possible changes in broader medical practices, institutional structures, value chains and business models.

This paper presents a theory-based view of what we term *digital drugs*, including how they embody benefit or value. The work is part of the scoping of a RCUK funded project addressing how, why and with what consequence medicines are

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[2] In this paper we use the word medicines and drugs almost as synonyms. We recognise however that they offer slight but significant shifts of emphasis. 'Medicine' evokes the practice of medicine and hence the practices of medicines, while drug evokes the manufactured product and its chemical character/materiality. Thus in this most basic sense the thing we address has an inherent multiplicity. The US National Library of Medicine thesaurus (MeSH – Medical Subject Heading) avoids this tension in its own way using the term *Pharmaceutical Preparations* – "Drugs intended for human or veterinary use, presented in their finished dosage form" (NLM - Medical Subject Headings – 2014 - Unique ID D004364 - http://www.nlm.nih.gov/cgi/mesh/2014/MB_cgi?mode=&term=Pharmaceutical+Preparations&field=entry – Accessed 15 Sept 2014).

digitalized. In contrast to the established view of medicines as artefacts located in a stage-based model of linear progression from drug development, through innovation and testing to approval and clinical use [5] this work sees drugs as constituted 'in-use'[6], as performed, and with their agency located and expressed within and as connections among sociotechnical and economic contexts. In the wider project we ask three primary questions: 1) what is a digital drug - exploring the conceptual and analytical shift from physical/chemical artefacts towards some digital sociomateriality; 2) how use-practices, markets and business models evolve for semi-configured and servitized kinds of medicines; 3) consequences for/changes in the 'wider whole' and the relations between the parts/players (pharma and health industries, payers, research, regulatory practices, patient-doctor relations, etc.). Cutting across these areas are multiple questions of *value*: therapeutic value, clinical value, health enhancement, value as management of risk or reduction of harm, market value, value in exchange, value in use, value for money, and ethical values.

Concept	**Definitions**	**Digital mechanisms**
Electronic prescribing (EP)	"The utilisation of electronic systems to facilitate and enhance the communication of a prescription or medicine order, aiding the choice, administration and supply of a medicine through knowledge and decision support and providing a robust audit trail for the entire medicines use process." (Connecting for Health, quoted in [7]) On DSS, see also: [8]. For an example of the application of DSS and EP in personalized medicine see: [9]	Decision support; error reduction; contributing to electronic patient record and Big Data repositories.
Stratified medicine (SM)	"Refers to the targeting of treatments (including pharmacological and non-pharmacological interventions) according to the biological or risk characteristics shared by subgroups of patients." [10] See also: [11] Often combined with, or used as synonym for *Personalized medicine (PM)*	"Targeting therapy and making the best decisions for groups of similar patients"; finding those who benefit most (or face greater risk), finding those who respond to *this* treatment.

Personalized medicine (PM);	"An emerging practice of medicine that uses an individual's genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease. Knowledge of a patient's genetic profile can help doctors select the proper medication or therapy and administer it using the proper dose or regime" (National Human Genome Research Institute, cited in [8]). See also: [12]	Targeting therapy and making the best decisions for a specific patient, on the basis of how the body will respond to treatment; selecting the right/best therapy on the basis of the patient's 'omics' and expected response to active ingredient(s).
Smart Drug Platforms (SDP)	"The same pharmaceuticals you take today, with one small change: each pill [contains] a tiny sensor that can communicate, via a digital health feedback system, vital information about medication-taking behaviors and body's response" (paraphrased from[13]). Also seen in wearable devices often linked to mobile phone e.g. Apple HealthKit.	Smart pills, smart patches (e.g.[14]). Devices and platforms for data acquisition and analysis. Tight feedback on medicines as released in the body.
Medical profiling(MP)	The process of determining a patient's 'omics' (a person's characteristics in terms of molecular components and biological pathways, such as genes, transcriptomic, proteomic, metabolomic, and autoantibody) for purposes of PM or SM [15]. See also: [16]	Informing SM categorizations and PM therapeutic decisions.
Value based pricing (VBP)	Payment to drug suppliers on the basis of the therapeutic benefit achieved. [35, 36]	Linking outcome data at patient level to payment; rebalance risk/reward
Pharmacovigilance(PV)	The assessment of the public health importance of potential new signals found in medicines-use data (e.g. adverse drug reactions) and the confirmation and quantification of risks identified and risk minimization measures (paraphrased from [17]). For an example of use of digital sources (e.g. social media) for this purpose, see [18]	Adverse event reporting systems, population scale outcomes data via EHR; prospective analysis.

Pharmacogenetics (PG)	"Examines inherited or acquired variations in genes that dictate drug response, disposition, or toxicity and explores how these variations can be used to optimize medication therapy." [19] Similar to PM and MP, but specific to genetic profile and pharmaceutical therapy.	Genomics and genomic profiling; epidemiological resources.
Anti-counterfeiting[AC]	Falsified medicines are fake medicines that pass themselves off as real, authorized medicines. Falsified medicines may: contain ingredients of low quality or in the wrong doses; be deliberately and fraudulently mislabeled with respect to their identity or source; have fake packaging, the wrong ingredients, or low levels of the active ingredients (paraphrased from European Medicines Agency web site). See also: [20]	Supply chain integration (bar codes, security codes; tamper proof packaging); consumer services (website seals/logos) and digital services.

Table 1: A sample of contemporary digital hybrids in medicines use

2 Origins and character of digital drugs

Medicines have always been hybrids (actor networks) - in part biochemical actor (active molecule(s)), in part material delivery system (pill, infusion, suppository, box, leaflet, cold chain), in part informational resources (representations and scripts to validate therapeutics and designate safe and appropriate use). And all bound up with complex and diverse social, scientific and economic interests and practices. However, the examples in Table 1 suggest that contemporary medicines in use become more materially, informationally and algorithmically complex, e.g. more digitally potent. We identify these as *digital drugs*[3] - that is:

[3] There is a possibility that something like a clinical medicine might emerge and be administered in a form that is essentially a pure digital phenomenon, e.g. an abstract 'program' of biochemical action to be compiled, 'downloaded' and 'run' in the body. More simply, a therapy such as a gym routine might be seen this way. For example the UK NHS 'Couch to 5K' is a therapy embodied in podcast downloads for achieving basic fitness through running [21]. A Google search of 'digital drugs' will also give information on possible audio-based psychotropic recreational drugs – so called 'digital highs'. In the sense that music can change your mood, perhaps even suppress pain, this is plausible. However, the general professional opinion is that the technology of 'binaural beats' is an interesting sensory phenomenon but psychotropically ineffective and that those who do get high are experiencing at best a placebo effect [22].

'drugs that are both dependent on and substantially constituted by multiple digital representations and connections, and whose use and effectiveness is strongly mediated through digital means'

The lens we use to study digital drugs is assemblage [23] – drugs as performed bundles of artefacts, interests and practices that connect and interact with wider wholes, including clinical work (use), research practices that validate utility/value and mitigate/metricate risk (clinical trials, systematic reviews, pharmacovigilance) and regulatory frameworks to guide practice (regulations, protocols and guidelines).

In using the concept of assemblage we follow the broadly Deleuzian approach [23, 24]. Assemblage signifies digital drugs as events and conjunctions in time and sources of qualitative difference (something happening, some things entangled, something noticed, something different, a process or processes at work, an enactment). In the Deleuzian vocabulary an assemblage is rhizomic, a question of emergence (emergent properties, generativity) in open systems – "the always-emergent conditions of the present" [23]. An assemblage is not then a 'thing' (as in a network), with specific life-span or essence. Rather, assemblage is understood in a metaphysics in which "the concept of multiplicity replaces that of substance, event replaces essence and virtuality replaces possibility" [25]. This implies actions and performance of complex and multiple causality/functional interdependencies (e.g. as a medicine is found in a body or bodies, modeled in a genomic profile, supplied, or prescribed), and is not tied to a fixed format or a single unambiguous event or outcome. This is in contrast to the term *hybrid* used here to refer to the (digital) drug as artefact and actor, including its mix of material/digital resources and its evolved

sociomaterial agency. We might say that *assemblage* is a concept applied to the 'instantiation' of the drug hybrid in use – the 'here and now' in a context (including in virtual contexts and in simulations).

We approach digital drugs by opposing the concept to its non-digital or pre-digital i.e. analogue version. The generations of medicines within our established regulatory structures, including the post-Thalidomide medicines, are essentially *analogue drugs* –seen as organic artefacts operating in an organic world of the body. Norbert Wiener, commenting on the probabilistic world of quantum mechanics, notes "the recognition of a fundamental element of chance in the texture of the universe" [26][p11]. In this sense anything analogue/organic is incomplete and uncertain ("...this random element, this organic incompleteness" [p11]). This 'incompleteness' certainly applies to medicines and their use. We are used to (or resigned to) the 'quantum' effect in medicines even as we strive for a stronger and stronger evidence base and thus certainty. Indeed the quantum is rather large given that most drugs prescribed to people do not work as desired most of the time[4]. Contemporary moves to digitize medicines may be seen as an attempt at closing down 'this organic incompleteness' within a digital certainty - e.g. through stratified medicine, genomics etc. as well as anti-counterfeiting systems or pharmacovigilance. It is tempting to imagine, as some proponents of these approaches do, that the shift to digital will

[4] The average NNT (Number Needed to Treat) for a licensed drug used in secondary care is well over 5, and for a prophylactic drug (e.g. aspirin for prevention of stroke) it may be well over 1000; that is over 1000 persons need to receive the drug, including paying for it and suffering possible side effects, for one to obtain a therapeutic benefit [27]. As a point of contrast everyday paracetamol (acetaminophen) which a dentist may give you after an extraction has an NNT of around 4.5 for post-operative pain [28].

drive down the quantum effect as it opens access to mechanisms that can validate actions and reduce error terms by orders of magnitude. This is not our position. Through the concept of assemblage, we argue, the quantum of the digital is made apparent, seen for example, in the simulated or more generally in the multiplicities that digital ontology accommodates.

Yoo's definition of digitalization recognizes this transition from analog to digital as fundamental: *'the encoding of analog information into a digital format and the possible subsequent reconfigurations of the socio-technical context of production and consumption of [the associated] products and services'* [29][p.137]. He proposes that such digitalization occurs in various ways: at the level of a physical object (e.g. a digital infusion pump in place of an analog gravity infusion roller clamp; a 3D tamper proof bar code on a package), at the level of digital/digitally mediated routines (a digital algorithm for prescribing; a smart phone app to raise adherence to therapy), or as new representations (a genomic account of personalized efficacy; a digital information resource on drug-drug interactions driven by massive electronic health records databases).

Any division between a digital drug (and digital quantum) and an analogue drug (and organic quantum) is not of course clear cut. Transitions occur over years as existing resources are reconfigured in digital forms and new resources added or retro-fitted. Our argument is, however, that as more of the active work we expect medicines to do (their agency) is (co)located in the digital, as digital resources and mechanisms are added and combined, and as this agency (re-)aligns to specific interests and goals, be they therapeutic, social or economic, then the nature of what a drug is, and how a medicine of medicines is practiced, 'tips' and something dis-

tinct and new emerges – a different kind of drug, a different set of practices, different assemblages. This in turn implies, we argue, new social, organizational and market structures.

Thus, as Yoo's definition of digitalization suggests and as assemblage requires, our interest is not focused ultimately on the digitizing of the information/object or the new digital routines or new representations, significant though these are - and of course we do need to consider the specific characteristics of digital products and services (as products/artefacts and as representations/services) and the 'bit string' economics that they obey [30]. But it is the 'subsequent reconfigurations' that are foreshadowed as seen in events and actions that we explore.

3 Three domains: (in-)use, research, governance

We approach digital drugs as assemblage from the perspective of three traditional domains in which they are by convention 'assembled' and within which issues of their value are addressed. These are the domain of clinical and therapeutic use, the domain of reflexive enquiry and research (gathering of 'evidence', knowing), and the domain of regulation and governance. These three domains are well established, each with its own practices and an established role/narrative as how we benefit (or not) from medicines. We do not consider here the biochemical domain, important though it is. These domains are of course interlinked, and one of the characteristics of medicines digitization is that these domains connect more and more e.g. events/assemblages are larger, stronger, richer, and more dynamic.

3.1 In-Use

As suggested above, digital drugs emerge in part out of efforts to computerize existing medicines use practices (prescribing, supply, administration, adherence, etc.) and in this way 'digitalize the object' with consequential ontological changes. Since the turn of the millennium it has been a key ambition of developed country health care policies to computerize prescribing in both primary care and secondary care and specifically to exploit the benefits of clinical decision support systems (CDSS) in helping prescribers select the right medicine for the patient, and to do so on the basis of a (digital) medical record (e.g. providing clinical data including in areas such as allergies), and data on recommended therapeutic strategies, available medicines, cost/cost effectiveness, and the effects of interaction among them (e.g. [31]). Similarly in the administration of medicines to or by patients, technological systems and devices such as smart pill boxes or text alerts are deployed to encourage or enforce adherence and record actual use [32]. Much of this work has necessarily been piecemeal (perhaps better described as 'targeted') as specific clinical practices and operational needs have been given computer 'support' (prescribing, dispensing, supply, administration, audit, 'academic detailing', phamacovigilance, etc.). CDSS are also understood as a necessary technological infrastructure, a necessary representation, without which a widespread application of personalized medicine cannot be contemplated [33], e.g. to enable the use in clinical practice of the 2500 genetic tests now already available [8] [34].

The potential *therapeutic value* and/or *service value* that motivate such projects include improved safety and reduction in errors and harm, more consistency of (good) practice, more efficient operations with less waste,

and better documented therapy. In this way initiatives to computerize medicines-use are by convention set against the familiar litany of contemporary existential health care problems: rising health care costs, unacceptable error rates and the harm they cause, demographic change, managing a growing burden of treatable chronic disease. Ambitions of progress in these areas are predicated on the existence of good informational infrastructures that represent valid forms of data (e.g. [35]). Many of these ambitions have not yet been fully met but the quality, coverage and scale of data infrastructures improves over time.

More system-focused policy motives reflect a desire for more *net value* (i.e. more health benefit and less harm) and *value for money* out of budgets for medicines. In the English NHS about 50 million population generate a yearly drugs bill of about £12bn. This leads to a perceived need to exploit digital technologies both to help control this significant line of expenditure and to increase the effectiveness of what is spent in improving health outcomes.

Models of the use of digital drugs and their regulation are founded on ideas of digital systems for establishing efficacy, expressing protocols and in the realization of individual patient's care pathways. This approach to medicines and their use is portrayed as offering a 'personalized' (or stratified) service (or services) wrapped around the medicine. Perhaps most significantly, the personalization process – the process to match your genetics and medical history, test results and other 'omics'[5] to what is

[5] Omics: a neologism used to describe a range of scientific fields (proteomics, genomics etc.) studying important biomedical aspects about a patient or patient group for subsequent use in personalised or stratified medicine; used also to refer to a person's

known about medicines and therapy - becomes a separate institutional endeavor. Thus a new industry of 'diagnostics' has emerged (with *economic value*) which serves through devices, tests, data analysis and protocols to control and target therapy choice and therapy delivery – generating a trajectory of events. This is an arena of practice in which the balance of business interests and clinical or public health interests is today unclear. More generally the development of an industry and services for diagnostics can be seen as an example of a 'service-dominant logic' (servitisation) [36] as a drug becomes less a standard product, and is more performed by a complex set of *value generating services* (*value* here being taken in multiple senses of the word; see above). The clinical utility of the therapeutic intervention (its relevance and usefulness in patient care [37]) "becomes a moving target" as information on its benefits and risks increases for groups or for individual patients [37]. As part of this, 'patients', their bodies and their carers may (but it is in no way inevitable) become more active participants in therapy, with their involvement too digitally mediated – a possible reconfiguration of the patient and their role as actor and information source (e.g. in consultations) to a data source (e.g. through wireless monitors or smart pills).

The health value a medicine generates, and the ability to identify this, becomes an open and multiple question – how to find a *value-in-use* (e.g. the model of a market in services, and in particular digital services). This moves away from traditional ideas of a *value-in-exchange* (the model of a market for products). This change in perspective is directly seen in con-

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characteristics in terms of molecular components and biological pathways (e.g. transcriptomic, proteomic, metabolom-ic).

temporary policy debates as national systems and payers consider 'value based pricing'– e.g. paying (or not paying) for the therapeutic service (or outcome), not for the molecule, and using a multi criteria algorithm and feedback to identify those that pass the value test and those that fail it [38, 39].

3.2 Research – evidence in the doing

A large armory of methods and techniques are today available to support scientific enquiry into medicines biochemical efficacy and other consequences and side effects (e.g. their validation as safe and effective) including statistical measures of outcomes as in a controlled trial, and synthetic metrics such as Number Needed to Treat (NNT) and Number Needed to Harm (NNH). These methods, refined in the past 70 or so years, underpin the established processes through which a new medicine is developed, tested and then licensed for specific uses. It is also the basis for the primary means by which a healthcare professional is given guidance on what medicines to use, when and how. Research findings are synthesized into protocols or guidelines for practitioners based on clinical data with or without some element of health economics (*value for money*).

In the UK for example, a national body - the *National Institute for Health and Care Excellence* (NICE) - prepares guidance on drug treatments which balances clinical and therapeutic benefits against cost[6]. Fundamental to this is the use of randomized control trials (RCT) and the types of

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6 http://www.nice.org.uk/guidance/index.jsp?action=bytreatment&TREATMENTS=Drug+treatments Last accessed 15 September 2014

knowledge that can be derived from trials, both individually and through meta-analysis (e.g. Cochrane reviews). It is in this way that we confidently (i.e. within confidence intervals, given the 'random element and organic incompleteness' of life) assert the therapeutic value and risks of a new medicine for specific conditions and/or subpopulations, or recompute them for older drugs. However clinical trials in their traditional form are increasingly considered unsuitable to obtain the evidence on benefits and risks of medicines tailored to specific individuals – for example a trial now has to assess both the efficacy of the treatment and the efficacy of the diagnostic that underpins the stratification, the co-dependent development of drugs and molecular diagnostics [40]. As Lewis et al (2014) suggest of personalized medicine "[It] forces us to question contemporary biomedical views of evidence, including its generation and use in decision making" [40]. There is thus a new focus on a set of complementary approaches to metricate value generated by medicines as they are to be used and as they are revealed through intensive digitization in the domain of use. Individual patient data collected/entered by clinicians at the point of care, or provided by the patient (now a data source), are aggregated into 'Big Data' as a potential basis for a new knowledge. A range of new analytic tools analyze or 'mine' these often non-standardized data and sift through the 'data turmoil' [41]. Among these analytic resources, for example, are new data-driven approaches to test the relationship between biomarkers and clinical outcomes [42] or for standardizing function instead of components in RCTs of complex interventions [43]. Alternatively, "real-time surveillance of individual patient outcomes" [37] may complement trials and improve evidence and support personalization. Drawing on digital resources, trials and experiments can be set up as "random-

ized studies embedded in routine care" through the use of electronic patient record databases [41]. Through such means the duration of trials and evidence gathering will shorten, some hope. For example, with an active distributed surveillance system in place "a full-scale observational study to evaluate the association between angioedema and drugs targeting the renin–angiotensin system was designed, conducted, and completed in 11 months" [44]. The perception of the need for such methods and the sense of urgency to exploit new research opportunities can be traced in part to the case of the pain killer and anti-inflammatory drug Vioxx. This medicine was licensed in 1999 and withdrawn in 2004. It took over 3 years and a number of patient deaths (disputed but probably in 6 digits [45]) before the negative side effects were acknowledged by the makers and the drug withdrawn from the US market [46]. The proposition is that, with digitalized patient records, and an effective and proactive pharmacovigliance system, such a case could be identified earlier with overall less harm. [44]

3.3 Governance and Regulation

Research designs reflecting digitization, as described above, imply significant modifications to regulatory regimes. Regulators have been among the most active in adapting to the new world of digital drugs. The FDA, the US regulator, has made many changes in its processes to accommodate a perceived new urgency in drug approval processes including a fast-track process for 'breakthrough therapies' [47]. There is a somewhat similar designation of 'orphan drugs' in medical areas where patient numbers are small and investments are unlikely to be made on the usual commercial basis. If and when medicines are fast tracked (a concept with a history

traced back to the early period of HIV/AIDS), and are expected to have a weaker research provenance at the time of licensing, they rely more on digital resources for monitoring of "post marketing safety and effectiveness" [44]. In such circumstances medicines-in-use data can serve to "raise or lower the level of concern about the overall risk–benefit profile of particular drugs", a capability that is described by the FDA as being transformational for the licensing process [44]. More generally they acknowledge the ability of these new resources of data to help fulfil the FDA's role. In the own words of the FDA, it has "evolved its regulatory processes in response to – and in anticipation of – scientific developments" [48], noting how it has responded to personalized medicines and the associated growth of diagnostic products by, "collaborating in key research, defining and streamlining regulatory pathways and policies, and applying new knowledge in product reviews" [48]. Meanwhile, Australia has, arguably, the first national framework to assess personalized medicine for coverage or reimbursement decisions [49].

As suggested above, digitization and the availability of data generated in clinical care practices (in-use) and held in national registries, migrate from a pure research (trial) status to embody more directly various interests including of health care system managers and the payers, patients and patient groups, and the pharmaceutical industry [50, 51]. That is, research in both new and old formats, and digitalized and synthesized prospective data sets become engaged in the systems of governance and regulation that surround medicines use. Research data thus will directly feed the development of detailed and comprehensive protocols of use (and non-use) for powerful and expensive drugs, described as frameworks for 'appropriate medicines use' [50]. Niezen et al. report research in The Netherlands

on registries (national databases of medicines use for a specific class of patient) as digital artifacts that are both an object to be managed, and an instrument to manage with. In this way clinical work (using medicines with patients and feeding the registry) and regulatory work (setting the protocol guidelines and reimbursement rules) become closely co-constitutive and co-evolving. In their analysis they question the desirability of a regulatory system that pursues a new 'digital objectivity' where available data embodies truth – as seen in many Big Data endorsements, and captured in the idea of the 'death of the denominator' when n=All (see also [52]). They contrast such digital objectivity with the more established 'regulatory objectivity', the kind of knowledge that is based on multiple evidential resources and embodies conventions and trade offs and collective expertise [53, 54].

3.4 Conclusion

In this paper we introduce the new concept of *digital drugs* as the intensified integration of digital services, data resources and algorithms into the practices of medicines. We anatomize it to reveal some of the main components (use, regulation, research) and mechanisms and relations using the lens of assemblage. The digitalization efforts that characterize the movement towards digital drugs are for the most part undertaken in the name of understanding, best practice, precision, and certainty. The individual initiatives and innovations described here can be seen individually as the expression of some regular and rational plan or policy to enhance the efficacy and efficiency of health care. Our view, our conceptual repertoire, and our chosen lens of assemblage, however, suggest something else or at least a different account of motivations and mechanism. As pro-

posed here, digitization (digital mediation of drugs) is pursued as a means to address the organic quantum of chemicals in the body. However, the complexity and multiplicity of elements that converge in or constitute a digital drug and its 'use/reuse' suggest that it need not, and perhaps should not, be seen as a pursuit of a certain or specific outcomes. Digital drugs are manifest as diverse, distributed, cumulated and dissected events and incidents across and between domains. They also permit multiple outcomes as data resources grow, algorithms learn and reconfigure, and virtual phenomena take new roles. Such multiplicity and instability is a price paid for the desired outcomes, for example in the case of in-use experimental designs or big data driven protocols (digital objectivity).

Markus and Saka introduce assemblage as a technique of collage and "something that generates enduring puzzles about 'process' and 'relationship'" and "[offers] an odd, irregular and time-limited object for contemplation" [23]. Applying it in these terms to medicines, this paper raises issues that might be assessed against a wider understanding of digitalization.

First, is the idea of digital drugs themselves, or more generally of movement (re-configurations) towards a digital materiality that attaches to and 'takes over' classes of artifacts. In this it recasts them ontologically away from an artefactual existence to one of assemblage - found in a complex ecosystem of data, algorithm and temporally unstable conjunctions, actual, real, virtual or simulated.

Second, and embedded within this perspective, is the question of the 'mechanisms' of the digital as rational processes of improvement, as (digital) controllers, as sensemaking, and as generative forces. Our case, and

the examples in Table 1, suggests that there is opportunity here for useful fundamental categorizations of this digital agency through artefactual and assemblage conceptualizations.

Third and finally, is the question of knowledge processes (research designs) as embedded in these phenomena. The methodological arsenal of the evidence based community (that of innovators, regulators and evidence-based practice) is changing and adapting. Event and transaction are at the core, able to be inspected, accumulated and animated in ways that were not possible in earlier eras. This reconfiguration is core to the phenomena of interest. But can the IS community reconfigure its research agendas and methods to meet this challenge?

Acknowledgements. We would like to thank the colleagues with whom we have discussed various ideas and aspects of this work and the anonymous reviewers who offered insightful comments on a previous version of this paper. We also acknowledge the research grant EP/L021188/1 (2014-2016) awarded by the Research Councils UK Digital Economy Theme to support this work.

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