

Applying Game Theory to One Health: Part 2: Modelling Human Healthcare Delivery



A classical economic view is that health system provision is influenced by macro-economic factors (market-led) and microeconomic factors (bottom-up/patient-led factors). Contemporary 'complexity economics' theories, however, are more applicable, whereby despite the macroeconomic factors imposed by governments or regulators or cumulative individual micro-economic decision processes, in practice a multitude of simultaneous decisions are occurring at many levels, which are influenced by multiple factors (which may not relate directly to the current health need) in a dynamic fashion. One classical economic assumption that would appear reasonably consistent is that most health-related decisions are made from a perspective of self-interest. However, there are vast numbers of participants with different perceptions of utility interacting daily in the highly complex system of healthcare delivery, thus the system continues to evolve to ever greater complexity of interactions. For the purposes of this paper, and to demonstrate the way typical decisions are made in healthcare delivery, a reductionist approach has been used to identify a small number of broad categories of participant and to ascribe general perspectives that each may have when interacting or making healthcare-related decisions.

Keywords: translational research; healthcare provision, One Health, healthcare economics

Each category of participant in healthcare differs in the way it attempts to maximise its own utility from healthcare. In the first paper in this series, the animal healthcare delivery sequence was modelled with particular emphasis on decision-making related to market penetration for new healthcare innovations and treatments. In this paper, the emphasis is on breaking down the complexities of human healthcare delivery to a simple sequence of events to understand the core transactions in healthcare delivery, as well as the points of influence or vulnerability.

The Participants in Human Healthcare:

There are six main types of primary participant in any healthcare process that are directly involved 'stakeholders' in each specific healthcare interaction, and each perceives the 'value' of healthcare differently. These are summarised as:

- I. **Patients** who primarily value the effectiveness of treatment measured by the extent of alleviation of a medical condition. However, they have to have the cost of treatment covered by their ability to afford it, access to public or private health insurance or charitable contribution. The extent that the cost of treatment influences decisions for the patient varies with the economic environment within which the patient exists.
- II. **Payers** who are primarily concerned with controlling the costs of providing treatment (e.g. Department of

Health and Social Security, insurance company, health management organisations, or the patient's own financial constraints if the patient is also the payer).

- III. **Primary influencers** who tend to value effectiveness above cost and have a strong influence, often via prescriptive control over the choice of treatment (e.g. medical practitioner, nurse, dentist, paramedical professional).
- IV. **Innovators** who consider the ultimate determinant of value to be the return on their own time and/or money invested (e.g. the pharmaceutical industry, researcher).
- V. **The regulator** (government agency) who places a broader societal value on the cost of treatment, and is primarily charged with protecting the safety of society and the patient population (e.g. national registration authority).
- VI. **Dispensers** who seek to make profit from sales (e.g. retail pharmacy, wholesaler, online order, supermarkets, herbalist).

Participants can be grouped into clusters each with sub-levels, all influenced by each other (Figure 1).

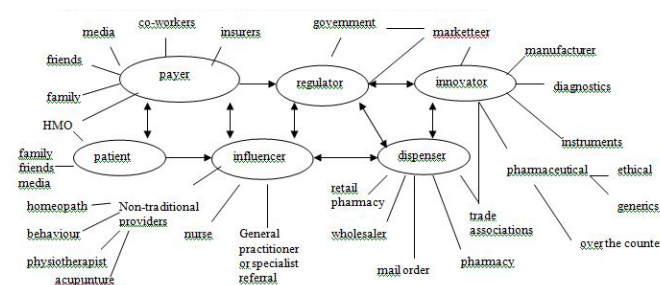


Figure 1: Clusters of influence upon each participant in the healthcare process

The fundamental activity around which all the participants interact is the decision of a patient to seek treatment for either a real or perceived illness, or to promote health. Without this, nothing else would occur. Even proactive screening / case finding approaches depend upon the patient once informed, seeking treatment, although this also illustrates the power of information to prompt the sequence leading toward a treatment decision. The process can be broken down into several component parts (see Figure 2) and is common to all healthcare provision. However, the way participants interact may differ across markets according to culture, infrastructure and other local factors. There are two supporting decisions: those decisions regarding cost and those impacting lifestyle which affect compliance with treatment regimens. Each step is also amenable to external influence from media or other entities that are not primary participants (stakeholders) in the delivery of specific healthcare objectives. The perception of a health-related 'need' is the starting point in this model. The patient is the primary decision-maker at this point, but others in the patient-payer clusters are secondary influencers, such as family, friends, and co-workers who do not have a direct 'stakeholder' involvement. The patient perceives a problem exists due to: signs of pain or discomfort; other visual signs; change in function; suggestion, such as through mass

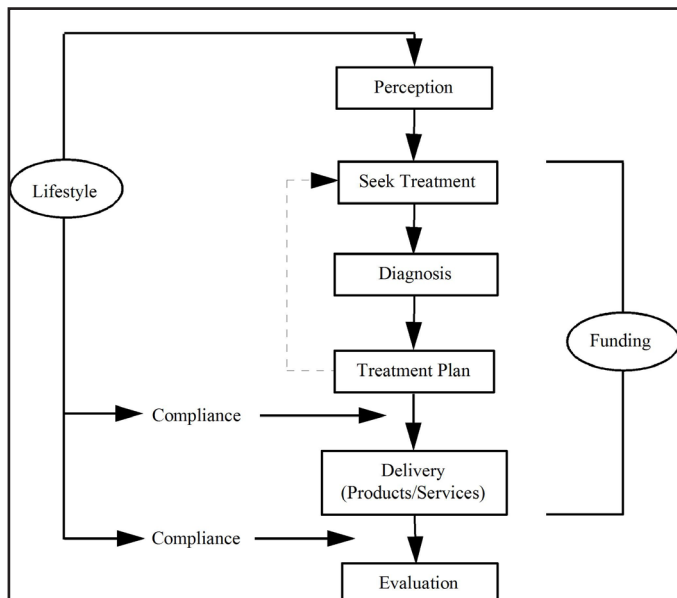


Figure 2. The healthcare process

media, or increased awareness due to education (from clinician, internet, reading, advertising, etc.).

Table 1 illustrates four categories which are ranked in order of the likelihood that a patient will recognise a condition and proceed to seek treatment.

		Ease of recognition of signs of disease by the patient	
		High	Low
Ease of raising patient awareness to signs of disease	High	1	2
	Low	3	4

Table 1: Two-way table illustrating the impact of raising awareness on patient decisions to seek treatment

Category 1 represents a condition that is easily recognised by the patient based on obvious symptoms and for which it is easy to raise awareness of the disease. An example could be urinary bladder infection (cystitis). For conditions in this category, a patient-targeted educational campaign is likely to be successful at developing the commercial market for treatment.

Category 2 represents the situation where it is easy to communicate the importance of the condition to the patient population but the patient may not be able to immediately detect the condition. If awareness is raised sufficiently, patients are likely to seek medical attention if they suspect the condition. An example here could be prostatic cancer, where 'difficulty urinating' can be easily communicated. Thus an information campaign orientated towards both the patient and clinician may be more applicable than solely targeting the general population, because patients with other urinary tract problems which do not require the treatment under consideration will also be presented.

Category 3 represents conditions where it is difficult to effectively communicate the forms that the disease may manifest, such as hormonal (endocrine) problems which can present in many forms. An example might be thyroid problems where over- or under-activity, or changes in sleep patterns and motivation levels, may drive a patient to seek medical opinion. In these cases, raising clinician awareness and provision of diagnostic backup and screening tests would prove more effective ways of promoting diagnosis

and treatment when patients present with variable symptomatology.

Category 4 represents diseases where it is difficult to raise awareness and patients may also not detect signs in the early (more treatable) phases of the disease. An example may be leukaemia, where there may not be any early signs evident. Raising clinician awareness through specialist education and introducing pro-active screening to detect onset before evidence of clinical signs may be the only ways of increasing early case presentation in this much more difficult sector.

Categories 1 and 2 can therefore be influenced more easily than 3 and 4, where it would be less easy to influence a patient to seek treatment. Category 3 patients are likely to be brought forward at various stages of disease, but it would more be difficult to target preventive measures for diseases in categories 3 and 4.

Once a patient recognises a problem, the decision is whether to seek treatment, then where to seek it. The factors influencing the patient to seek treatment include: perceived potential severity of illness – death; disability; cost; accessibility; the belief that something can be done. Once the decision to proceed with medical care has been made, the payer becomes a primary decision-maker. Where the payer is the patient, the patient can maintain decision-making power. The decision at this level is influenced by cost, access and belief that a certain type of provider can help. Where the payer is another body, e.g. insurance company, health management organisation or government, the decision is influenced by "programme rules", which restrict access to some types of providers and restrict treatment options available to the patient. The patient may also decide to become the payer to regain control of their healthcare decisions. The payer's decisions are influenced by considerations of their own total cost and perceived treatment quality, which is rationalised in terms of cost versus benefit.

Socio-economic status and belief systems are therefore relevant (Table 2) when trying to distinguish between high-cost, high-quality treatment and low-cost, low-quality treatment. In serious conditions, it is likely that the balance of opinion will favour high-quality treatment if their belief is that the condition is curable. In less urgent or less severe conditions, alternatives may be sought (e.g. pharmacy advice or self-medication) and the trade-off may be consciously made to seek a lower cost and lower perceived quality (and possibly effectiveness) of treatment by both the patient and the payer.

		Cost of visiting provider	
		High	Low
Perceived quality of treatment	High	2 or 3	1
	Low	4	2 or 3

Table 2: Two-way table illustrating likely treatment quality preferences based upon the cost of a healthcare visit

Once the presenting complaint of the patient has been evaluated, a diagnosis should follow. If the patient has decided to seek treatment within the medical provider network, the primary decision-maker based upon their expertise becomes a healthcare professional (e.g. a doctor). In markets where patients can readily self-treat, or where a problem is not perceived as severe and where over-the-counter products are available, this role may be filled by a pharmacist or para-medical healthcare provider. The factors influencing the medical practitioner's diagnosis

are: experience, continuing professional development education, influence by pharmaceutical manufacturers, professional bodies, payers and the general media. The concept of complexity economics is well illustrated in these scenarios which correlate with the patient's self-perception/self-diagnosis of their problem, which is a function of personal experience, education, word of mouth, trust in healthcare providers and the wider clusters of influence (see Figure 1) notably including media influence.

Once a diagnosis or differential diagnoses have been generated, a treatment plan is established. The treatment plan, in some cases, creates a loop back to the "seek treatment" decision (see Figure 2), such as when the treatment plan of a medical practitioner comprises referral to another professional or where an alternative/differential diagnosis will be followed up. The treatment plan from medical practitioners can include a combination of: pharmaceutical interventions (both prescription or non-prescription); nutritional changes; behavioural modification; surgery, or referral to another provider. These options are not all available to a patient without involvement of a medical practitioner. The patient influences the practitioner by providing information concerning personal wishes or the likelihood of compliance with the treatment plan. Yet the medical provider's treatment plan decision has to be cognisant of likely effectiveness, safety and cost. The payer exerts influence on the medical provider and patient and may restrict the use of certain interventions, or require a specific sequence of treatment interventions. The payer's programme rules focus on cost, efficacy and safety and, if a public funding agency or private insurer, typically aim at limiting overall cost from a population perspective (as opposed to a case by case). The regulator's decisions are also designed to maximise the utility of the total population, rather than individuals. These decisions are a function of the "risk" the regulator is willing to take. The regulator can either take the risk that a valuable, safe treatment is kept off the market, or they can take the risk that an unsafe treatment is placed on the market (i.e. a type 1 or type 2 error). Regulators are also very cognisant of cost and use a variety of cost-benefit, cost-minimisation and qualitatively-based cost-effectiveness studies to determine public funding models for medical technologies. These in turn significantly influence the incentive for medical research directions. Aware that not all benefits can be neatly captured as a financial figure, subjective measures such as Quality Adjusted Life Years (QALY's) are used to give weighting to value perceptions by society. However, in OECD countries, where governments typically cover 80% of individual healthcare costs and spend over 15% of government revenue on the healthcare of citizens, cost is a limiting factor and will in future years be a major determinant of the scope of publically funded health provision.

When a pharmaceutical product is part of the treatment plan, there are three relevant decisions to be made by the practitioner:

- which class of drugs is appropriate for the plan?
- which specific molecule is appropriate?
- which brand in a generic environment (based on cost/brand recognition)

The product that the provider will choose is influenced by the effectiveness of treatment, the cost of treatment and the ease of distinguishing a product from other products with the same or similar indications of use. Tables 3 and 4 give examples of the ways pharmaceutical innovators are influenced by market conditions to maximise the uptake and profitability of a new product.

		Efficacy of treatment	
		High	Low
Cost of treatment	High	2	4
	Low	1	3

Table 3: Two-way table illustrating a ease of market penetration (1 = easy, 4 = very difficult) based upon criteria of treatment cost and efficacy

Ideal for the patient would be a highly efficacious, low-cost treatment (category 1), however, highly efficacious products are generally premium-priced (category 2). A high-cost, low-efficacy product would not be well received by the market, given accurate information. If distinction cannot be made based on cost as in Table 3, branding strategy and advertising will play an increasingly important role in distinguishing one product from another (Table 4).

		Cost of treatment versus rival product	
		High	Low
Ease of distinguishing product from rivals	High	3	1
	Low	4	2

Table 4: Two-way table illustrating ease of market penetration based upon branding and treatment cost

Thus, in order to influence the level of demand for a new product, some basic criteria need to be fulfilled:

- Easily distinguishable option with few or no rival products and preferential pricing or superior efficacy.
- Where there are many generic rival products of equivalent efficacy, the product needs to represent an easily discernible option or cost less.
- Where there is little direct competition, but many alternatives, clear product distinction will have to outweigh relative costs.
- In a high-competition market, with many alternatives and where pricing is not favourable, this represents a very difficult market environment in which innovative focus has to be upon production and manufacturing processes to decrease cost of production.

The patient's decision to comply with a treatment plan is an important determinant of outcome and it is important that the plan is agreed between all involved participants in advance to ensure it is sustainable.

Pharmaceutical innovators target the needs of the patient, medical provider and payer in an attempt to balance the cost of development against the anticipated sales and opportunity cost of other projects not progressed in consequence. Keeping a balanced portfolio is an important part of managing the risk of product development. Where several leads are generated from the same innovation platform and only a couple can be pursued, the implication is that the opportunity cost might be as large for the candidate which is not chosen for development as for the lead candidate. Table 5 illustrates the type of prioritisation process required when balancing research and development costs against potential market value.

		Market value	
		High	Low
Cost of development (measured in time and finance required)	High	2	4
	Low	1	2

Table 5: Two-way table illustrating the overriding aim of research and development activities

There is a trade-off when balancing high cost and high market value against low cost and low market value (both prioritised as category 2). This decision will be partly based upon the cost: benefit ratio of each, the opportunity cost and risk management in terms of probabilised success, portfolio management and overall potential earnings of the project given similar profitability.

The delivery of a service or a product is instructed in the treatment plan. The delivery of a pharmaceutical product to a patient according to a treatment plan includes three things: the drug, a delivery mechanism and information about the drug. The primary participant at this stage is the dispenser. The dispenser can be a retail dispenser – which includes a stand-alone pharmacy or a pharmacy as part of another retail business (grocery, department store, etc.), a medical practice, a hospital, a specialist practice, online order, etc. The influence the dispenser has is a function of which type of dispenser they are and the local regulations governing their activity:

- Retail dispensers generally have no decision-making authority. They can influence the patient when the product is multi-sourced and will inform the patient about cost or plan options when relevant.
- The medical practitioner as a dispenser has decision-making authority over delivery of the drug. This decision-making ability may be constrained by the payer through social security or insurance reimbursement rules.
- Online/internet dispensers have influence similar to that of a retail dispenser.

The influence on drug delivery decisions is primarily a function of the dispenser type's profitability. In other words, if a dispenser has the freedom to influence a patient, how they choose to influence a patient is driven by what is most profitable for the dispenser. The dispenser may also be influenced by concerns for the patients' cost in a competitive market. The delivery decisions influenced by the dispenser are primarily decided on by the payer and the patient. The regulator has decision-making authority over the types of pharmaceutical dispensers that exist in a given market.

A key determinant of success for a pharmaceutical company is developing an ability to target, understand and in some cases influence each of the decisions in the transaction. Figure 3 is a worked example, where the probability of each set of decision choices has been set at parity (e.g. 50% chance of choosing to treat versus not treat, or a 33% chance of choosing between three possible providers of treatment, etc.). The exact trend can be established by local market research and each of these sets of decisions can be adapted according to concurrent trends. Through education or awareness campaigns, it can be made more likely that once 'breast lumps' are detected by a woman, treatment will be sought. With appropriate preventive health strategies, this decision could realistically be raised to over 95% seeking some form of advice or treatment versus 5% those choosing to ignore the 'lumps' completely, with a further 5% choosing either 'self-treatment' or a non-medical provider. In the case of treatment for mild urinary tract symptoms, however, education campaigns could also be used to influence people *not* to initially seek treatment from a medical provider and the option, set arbitrarily at 33%, may become only 10% when patients are aware of a threshold of symptoms that require medical intervention rather than home-based management. In doing so, self-medication could be increased to account

for the majority of treatments, increasing over-the-counter sales and taking the expense of medical consultation out of the system and freeing up medical capacity. The rate and types of product adoption can therefore be influenced. This type of model, even in the scenario suggested by complexity economics, can rationalise behaviours and help target resources to maximum effect. In the medium term, this game-theory approach will become increasingly evident as efforts are made to constrain increasing costs within stagnating public healthcare budgets.

Figure 4 uses typical decision proportions as based upon our medical practice and illustrates how the probability of different outcomes can be greatly altered, mainly via patient education and the attitude of the influencer (ie doctor or non-medical provider). The proportion not receiving a formal medical procedural work-up was halved (14%) in this example, which is important in potentially serious medical conditions like breast cancer, and the number of interactions that resulted in a medical procedure* was increased by well over five-fold (76%). The probably of no treatment or further investigation was decreased from 56% to 10%, which may better reflect the low-risk subset of young women with benign 'normal' fibro-adenomatous breast changes.

The influence could just as easily have been used in the opposite direction to decrease medical interventions. A good example of this in our practice has been the substantial decrease in rate of antimicrobial prescriptions and increase in alternative management methods via targeted strategies aimed at influencing demands of patients and payers and the attitudes of the influencing healthcare professionals. During a treatment plan and after completion, there must be evaluation of the plan's effectiveness in solving the problem identified during diagnosis. The patient is the primary decision-maker with regard to whether or not a treatment plan has worked, and evaluates efficacy in relation to their expectation and the

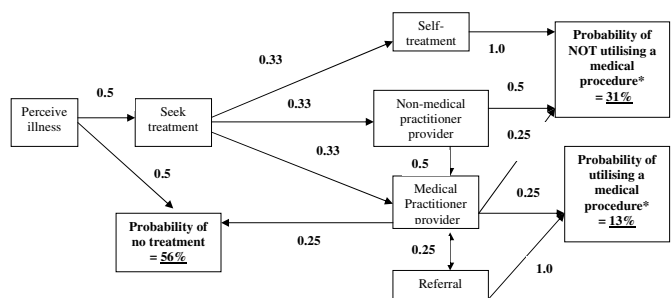


Figure 3: Worked example of a decision cascade from the point of perception of illness through to dispensing of therapy with all decision probabilities set at parity.

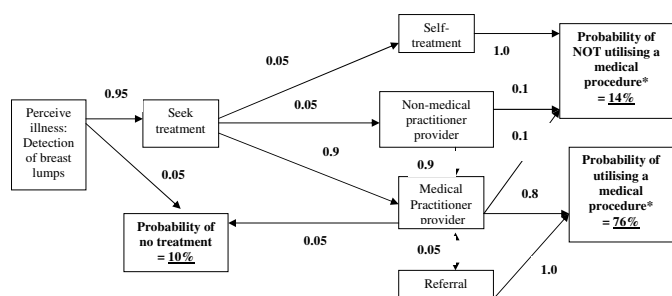


Figure 4: Illustration of an 'influenced' decision cascade showing how health outcomes can be altered to favour medical procedural follow-up (e.g. breast lumps detected by patient)

total cost of treatment plan (including opportunity cost and impact on lifestyle). Patient evaluations are based on: symptomatic relief, ability to resume normal activities or demonstrable change in the condition (e.g. tumour shrinkage). The clinician co-evaluates a treatment plan based on their medical evaluation, the patient's own evaluation, repeat investigations and empirically upon whether any better outcome could be hoped for using existing alternative treatments.

The clinician only has the potential to evaluate a plan if the patient returns to the provider after the treatment plan was implemented. So, in many cases the clinician must assume a result which may over-estimate efficacy with the common assumption that lack of re-presentation of a patient equates to a cure.

Discussion

The patient has a great deal of influence over the entire process and typically controls whether or not a healthcare transaction proceeds at all. If the patient does not perceive a problem exists, nothing happens. But just because an illness exists and is recognised, it does not mean treatment will be sought. Lack of awareness of solutions, denial and fear of the consequences are all relevant factors (Reeve-Johnson, 2003). The more difficult a problem is to perceive, the less likely treatment will be sought. When it comes to deciding where to seek treatment, the patient has a variety of choices and can choose to stop and exit the healthcare provision system any time. Medical practitioners in general practice are important influencers, with substantial numbers of patients waiting to receive treatment, however, having sufficient time to explain the disease, to share the options for treatment and internalise the decision into a collaborative disease management effort in which the

patient is fully engaged and therefore more likely to comply with the regimen, is important. It is helpful at this time to discuss the realistic expectation for benefits and side-effects, as well as the consequences of not completing treatment. By virtue of improving compliance with the treatment protocol, the patient is more likely to benefit to the full extent from the treatment.

Pharmaceutical companies are fully aware of the transactional nature of healthcare, yet many other participants in the system may not perceive the economic fundamentals as clearly. The patient has a very large amount of influence over the transaction as a whole. If a problem is not perceived, or treatment is not sought, then no sale will occur and innovation will not be utilised. The patient's decision-making capability or influence is constrained by clinicians and payers, but in different ways for different reasons. The clinician's influence over the patient is primarily due to either their expertise or through access to products limited by prescription. The patient believes he is not qualified to identify and solve certain medical problems, and so gives control of this decision to the expert. The clinician tends to be the decision-maker at the diagnosis stage and to be the primary decision-maker at the treatment plan stage, but is constrained by the payer. Clinicians can influence patient selection at the perception or seek treatment stage through screening (e.g. faecal occult blood screening, PAP screening, blood profiling, etc.). The level of information provided on the treatment options has a large effect at this stage. Table 6 summarises the key decision-makers at each level of the healthcare transaction and who influence the progression through a series of decisions common to most modalities of healthcare.



PARTICIPANT/STAGE	PATIENT	MEDICAL PROVIDER	PAYER	DISPENSER	REGULATOR	INOVATOR/MANUFACTURER
PERCEPTION	Primary decision-maker	Influence through screening	Influence by paying (or not) for screening			Influence via awareness campaigns
SEEK TREATMENT	Primary decision-maker	Influence via availability and cost			Influence access and availability	Influence via educative campaigns
DIAGNOSIS	If self-treating then decision-maker	Primary decision-maker		Influence in self-treatment situation		Influence via education provision of diagnostics
TREATMENT PLAN	Influence through opinion and requests	Primary decision-maker	Secondary decision-maker, influences through reimbursement rules	Primary/secondary decision-maker in self-treatment situation	Tertiary decision-maker, controls band of possible treatments	Influence primary decision maker regarding selection of product and its inclusion in treatment plan
DELIVERY				Primary decision-maker	Influence type of dispensers & level of control	
EVALUATION	Primary decision-maker	Secondary decision-maker - if patient returns for evaluation				Influence through helplines and making comparative data available
COMPLIANCE	Primary decision-maker	Limited control	Influence through ease of payment and level of cover			Influence through education and helplines

Table 6: Summary of the primary decision-makers and main influencers during the healthcare process

The patient allows the payer to exert influence for economic reasons and cedes a degree of control to the payer in return for the payer's role in bearing some of the patient's costs. The payer, however, does not make decisions on a real-time basis, like the patient and provider. The payer acts on the decision in advance, through a set of programme rules.

Healthcare provision systems are dynamic and evolve towards greater complexity as the number of influencing factors accumulate in the absence of any single macro-economic control point. Because new possibilities are always presented (innovations, management efficiencies, disease outbreaks, capacity issues, funding, communications, regulations, etc.), the system can never reach stable equilibrium. Changes occur regularly and those that do not broadly increase utility for all participants will ultimately be rejected.

Summary

- Provision of healthcare is fundamentally a complex transaction between a relatively small number of core stakeholders and a multitude of external influences, including belief systems which do not necessarily relate directly to the immediate healthcare need.
- The participants in healthcare interact and rationalise their perspectives of utility through a form of economic exchange which is constantly evolving to greater complexity to cater to increasingly diverse influences.
- Interactions between social, psychological, environmental and physical determinants of health mean that for patient education to be effective, it has to be targeted to cater to messages that are easily communicated, signs that are easily recognisable and messages that are contiguous with belief systems and perceptions that may not relate directly to the current healthcare issue.
- Patients and healthcare professionals may be less aware of the underlying economic imperatives and ways these are influenced, than pharmaceutical companies, dispensers, insurance and government funders who have evident economic motives.
- In the healthcare industry, demand generally pre-exists and education, awareness, media constructs and

supply of treatments influence the way new products and interventions are utilised.

- Central to healthcare provision is the individual adoption process of the patient, which includes the perception of illness, the decision to treat, diagnosis, setting up the treatment plan, the delivery of the drug and evaluation of the effectiveness of the treatment plan which impacts compliance. Each of these steps is a potential point of influence and can be used to influence the choice and extent of medical intervention to either increase population health or manage demand within the capacity constraints of the healthcare systems.
- Complexity economic models are highly relevant to health delivery because healthcare systems are dynamic and continually evolving to accommodate new possibilities through innovation, efficiencies, funding changes, communication and other factors. A stable equilibrium is never attained and changes which reduce the utility of any participant group are likely to be rejected.

REFERENCES

1. Reeve-Johnson, L. (2003) Quantifying and maximizing the value of innovation in the pharmaceutical industry. *J. Vet. Pharmacol. Therap.* 26 (Suppl 1), 19-55.
2. Reeve-Johnson, L. (2015) Translational Research: putting the right price on innovation. *Vet. Record* 173: 312-313.
3. Reeve-Johnson, L. Chapter in *Practical Veterinary Forensics*, ed. Bailey D. (2016) Macro-economic incentives for Translational research and One Health collaborations. CABI publishing, Cambridge.
4. Reeve-Johnson, L. (2017) Applying Game Theory to One Health: Part 1: Modelling Veterinary Healthcare Delivery. *IAJH*. Vol 3. Issue 4. 16-21

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