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Innovative Applications of O.R.

Understanding foodborne transmission mechanisms for Norovirus: A study for the UK's Food Standards Agency

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ABSTRACT

The paper outlines the 'complete arc' of a range of modelling activities initiated by UK's Food Standards Agency (FSA). Norovirus produces infectious intestinal disease in humans via both person-to-person contact (P2P) and foodborne (FB) transmission. The FSA commissioned a research study to improve understanding of FB mechanisms, and of where it might target its efforts. In response, an existing P2P model with a single, exogenous parameter for FB transmission was transformed into a System Dynamics model of FB processes. The modelling involved individual interviews and a facilitated group modelling session, the FSA providing access to relevant experts. Contamination routes modelled concerned: bi-valve shellfish; sludge; some fruits and vegetables; other foodstuffs. This large model showed it was possible to give an account of the underlying causal mechanisms; and it facilitated a categorisation of parameters in a manner useful in agenda-setting for future research and in identifying policy levers. Some creative thinking extended the work in an unexpected but significant way. Data and mathematical analysis made it possible to calibrate a P2P model for the first time. Sensitivity analysis then suggested that small changes in human behaviour could explain the tenfold seasonal variation in Norovirus cases, and also offered an understanding of the relative importance of FB and P2P vectors. The range of consequences of the study included an increased understanding by the FSA of the different means of trying to control Norovirus, practical actions and ideas for further work.

1. Introduction

Norovirus can cause very unpleasant intestinal illness in humans. Norovirus – NV – is commonly called the 'winter vomiting bug' because of its strong seasonality (Campbell, 2018; Donnelly, Kirk, & Scott, 2018; Emmot, 2017; Press Association, 2016). It produces very unpleasant symptoms and can be contracted by most people, even the youngest and fittest, as seen in the outbreaks at the World Athletics Championships in London in 2017 which caused competitors to withdraw from events (BBC, 2017; Public Health England, 2017) and amongst security staff at the Pyeongchang Winter Olympics (BBC, 2018a). The UK is thought to experience around three million cases per year (Tam, Rodrigues, & Viviani, 2012). Globally, NV results in almost 700 million annual cases (95% CI: 489–1086 million) and 220,000 deaths (95% CI: 171,000–277,000) (Bartsch, Lopman, & Ozawa, 2016).

Viewed in narrow financial terms, NV costs the UK NHS ~£80 million annually (Tam & O'Brien, 2016) whilst global costs are estimated at $60 billion (95% CI: $44.4–$83.4 billion) in: direct health care costs; lost productivity; and mortality (respectively 10%, 45% and 45% of the total).

However, the fact that NV-related illness is self-limiting and usually non-fatal means that it "has received comparatively less attention than other infectious pathogens" (Bartsch et al., 2016, p. 1), a comment that holds true from both a public health and a modelling perspective. This paper is focussed on NV. It concerns OR work on the mechanisms and consequences of the foodborne transmission of the virus. The aim here is to present the 'complete arc' of the work, from commissioning to implemented actions: the broad context, the commissioning of a research study by UK's Food Standards Agency, the creation of a large model (and the process used to accomplish this), the extension of the modelling in a new direction, the contributions and recommendations that flowed from all of this work, the FSA's own peer review of the modelling, and the practical actions and ideas for further work.

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The contributions of the paper are as follows. Work using System Dynamics on the detailed modelling of FB transmissions demonstrated the effectiveness of a combination of individual sessions with domain experts and a facilitated group modelling session, resulted in the first ever model of these mechanisms, and proved useful in agenda-setting for future research and in identifying policy levers. An unexpected extension of the work produced further contributions. Mathematical analysis of a reduced model produced the first empirically-grounded calibration of a 'person-to-person' model for Norovirus. For the first time this gave the FSA a quantification of the scope of P2P and FB effects. This model generated innovative insights into the observed seasonality and the relative importance of transmission vectors and produced increased understanding of ways of controlling Norovirus.

The paper proceeds as follows. Section 2 sets the scene for the study by outlining the main features of NV, the role of the Food Standards Agency and the aims of the research study. The modelling work is then presented in the following two sections. Section 3 describes the creation of a large System Dynamics model which included a fully endogenised formulation of the main foodborne transmission mechanism of NV, and outlines how this model contributed to increased understanding of the virus. Section 4 describes how mathematical calibration and analysis were used with a compact model to give insight into the extreme seasonal variation in NV cases and pose significant questions for the FSA regarding the best means of controlling NV incidence. To complete the 'arc', the paper closes by exploring the recommendations, the FSA's positive review of the work, and the consequences.

2. Background

This section sets the scene for the work. The first two subsections outline the background, and background literature, of Norovirus and of the type of modelling used. The final sub-section describes the organisational setting of the study.

2.1. Aspects of Norovirus

Noroviruses are segments of RNA inside a protein coat, or capsid. Noroviruses arise in four genera of the family *Caliciviridae* (Thiel & König, 1999). These are simple sub-microscopic entities, about ~30 nanometres (3×10^{-8} m) in size. They only replicate inside living host cells: the surrounding proteins bind to receptors on the surface of host cells, penetrate the host and accomplish RNA replication using the host's own cellular machinery. New, protein-coated virus particles are synthesised and then released.

Norovirus is an enteric pathogen: in the human intestinal tract it produces intestinal disease (Glass, 2013). NV has a complex protein structure: based on its amino-acid sequence, it is classed into seven genogroups: GI to GVII. Form GII.4 is the most frequently occurring in humans (Vinjé, 2015; Zheng, Ando, & Fankhauser, 2006).

Detecting NV in humans is problematic as viruses are difficult to culture but there are increasingly successful applications of the technique 'reverse transcription-polymerase chain reaction' (RT-PCR) which allows detection of the NV genome from a faeces sample (de Leon, Matsui, & Baric, 1992; O'Neill, McCaughey, & Coyle, 2002; Vinjé, 2015). However, because of the range and ambiguity of symptoms, and because NV can be detected in healthy individuals, it is not always possible to be certain that NV is the underlying cause.

Humans exposed to NV have a latent period of roughly two days before illness manifests. Most then experience some or all of the following: very sudden nausea, explosive vomiting, diarrhoea, abdominal pains, stomach cramps, headaches and fever. Such people are highly infectious; most recover after two days (Kapikian, 1996). The main effect of NV is the morbidity of those symptoms. Although it can be hard to ascribe individual deaths definitively to NV, mortality can result. For example, young children experience more severe symptoms of gastrointestinal disease (Huhti, Szakal, & Puustinen, 2011) whilst the elderly frequently have other conditions which NV may exacerbate (Koopmans, 2009).

The main vector for NV is person-to-person contact involving an NV sufferer – 'P2P'. Small amounts of faeces or vomitus may be ingested. Only a very small number of NV particles (perhaps only 10–100) need be ingested for transmission (Caul, 1996; Kapikian, 1996). For comparison, a gram of faeces can contain 10 million NV particles. Such P2P transmission results from: the ingestion of particles picked up via direct physical contact (a handshake, changing a baby's nappy, assisting an infected person whilst providing care); or from oral or nasal ingestion resulting from aerosol transmission which can occur half metre away, possibly more (Barker & Jones, 2005; Bonifait, Charlebois, & Vimont, 2015; Marks et al., 2003); or via contaminated surfaces (the door handle in a lavatory, a light switch). Transmission can also occur when cleaning up the vomit or faeces of sufferers.

Although NV cannot replicate without a host cell, it can survive for long periods outside an organism. Consequently, transmission between people is sometimes indirect, via food, or water, or a 'fomite' (an object or material). Hence, although there is some conceptual overlap (Bull, Tu, & McIver, 2006), the literature labels transmission as occurring primarily via two routes; P2P and FB.

Cooking partially or totally reduces NV viability, thus reducing the probability (and possibly the severity) of any infection (Bertrand, Schijven, & Sánchez, 2012; Tuladhar et al., 2012). However, this still leaves routes by which infected humans can pass NV particles via the food chain (Koopmans & Duizer, 2004; Rzezutka & Cook, 2004). These are described in Section 3.

Norovirus is a significant cause of foodborne disease. In the US it is the main cause (Batz, Hoffmann, & Morris, 2012; Saupe, Kaehler, & Cebelinski, 2013). In the UK its 73,000 cases made NV the UK's third most common source of foodborne disease after *Clostridium perfringens* and *Campylobacter* (Tam et al., 2012).

The social mixing, foodborne and sudden onset aspects of NV lead to its association with outbreaks on cruise ships (Neri, Cramer, & Vaughan, 2008; Pearlman, 2017; Verhoef et al., 2008; Widdowson, Cramer, & Hadley, 2004), in restaurants (for a high profile case in the UK see Health Protection Agency, 2009; Meikle, 2014), and in hospitals and residential homes (Health Protection Agency, 2012; Iturriza-Gomara & Lopman, 2014; Kambhampati, Koopmans, & Lopman, 2015; Meakins, Adak, & Lopman, 2003). Hospital outbreaks can increase patient waiting times (Marsh & Duncan, 2018) and even lead to hospitals refusing further admissions and the deep cleaning of wards (BBC, 2018b; King's College Hospital, 2016; Mahncke & Geisler, 2016). Incidence frequently spikes around Valentine's Day, possibly linked with oyster consumption (David, McIntyre, & MacDougall, 2007), and has a strongly seasonal pattern (see Fig. 1) observed in a range of countries (Ahmed, Lopman, & Levy, 2013; Lopman, Adak, & Reacher, 2003; Spiegel Online, 2017).

Norovirus is the most commonly identified cause of infectious intestinal disease and acute gastroenteritis in Western Europe and the US (Fankhauser et al., 2002; Hall, Lopman, & Payne, 2013; Koopmans & Duizer, 2004; Lopma et al., 2002). In the developing world NV produces even more significant effects, in terms of gastroenteritis and child mortality caused by diarrhoeal-related illness (Ahmed, Hall, & Robinson, 2014; Lanata, Fischer-Walker, & Olascoaga, 2013; Siebenga, Vennema, & Zheng, 2009). In developed countries there is considerable under-reporting: sufferers may not seek medical care because symptoms end quickly (Bernard, Werber, & Höhle, 2014; Tam & O'Brien, 2016), plus GPs do not always diagnose NV (Scallan, Hoekstra, & Angulo, 2011). Nevertheless, the UK's estimated three million annual cases and the six million days

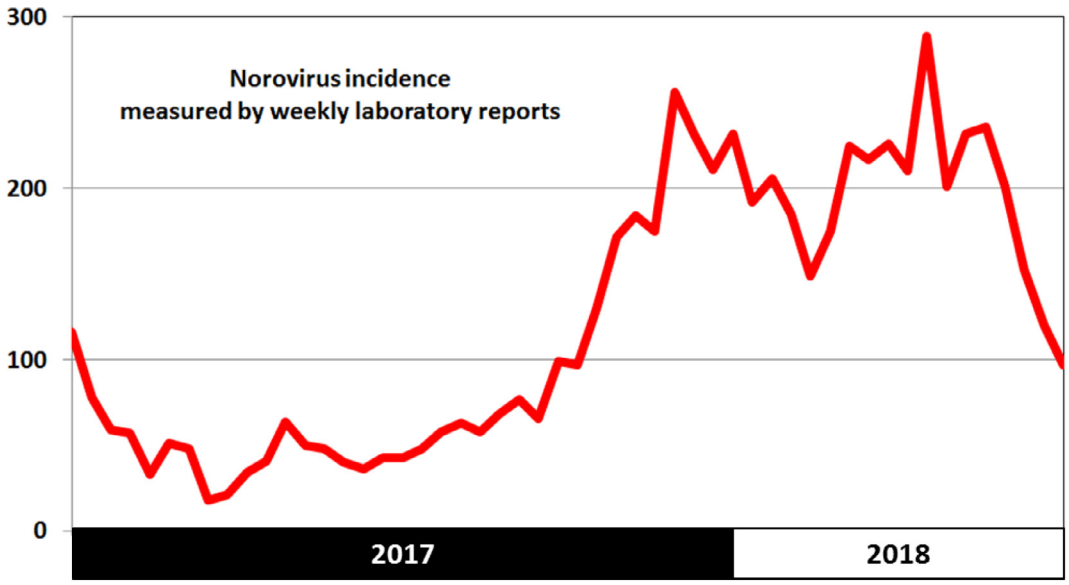

Fig. 1. Seasonality of Norovirus. Incidence in England and Wales for a one year period covering the recent winter of 2017/18, as measured by weekly laboratory reports confirming presence of the virus in referred cases. The data is provisional but any changes are likely to be minimal and to apply to the most recent part of 2018. Adjusting for estimated under-reporting and demography means that a constant figure here of ~200 corresponds to ~3 million annual UK cases. Data source: Public Health England.

of the highly unpleasant 'experiences' described above merit some attention.

2.2. Type of modelling employed

In purely mathematical terms, the core modelling approach and formulations used in the paper are derived from mathematical biology and epidemiology. The compartmentalisation of humans into those who are disease-free, are subsequently in various stages of experiencing the disease, or have experienced it, appears as a variation on the standard SEIR structure. The work also uses the diffusion idea, by which infection occurs via the social mixing of those with and without a disease. These two formulations are well-established (Anderson & May, 1991; Murray, 1989). They are also frequently employed in general OR modelling studies, where variants and/or more complex versions of the same ideas are crafted for specific disease situations; for recent examples, see (Araz, Lant, & Fowler, 2011; Büyüktahtakin, des-Bordes, & Kibis, 2018; Griffiths, Lawson, & Williams, 2006; Liu & Zhang, 2016; Shamsi, Ali Torabi, & Shakouri, 2017). The same can be said of studies using System Dynamics (Bennett, Hare, & Townshend, 2005; Evenden, Harper, & Brailsford, 2006). However, within the System Dynamics field a link to the work of Bass (1969) is made. Hence, the 'generic' nature of the diffusion structure is seen not just to apply to susceptible and infective humans and diseases but to those who are potential and actual adopters of a specific behaviour, for example the take-up of a medical technology (Homer, 1987) or of product innovations (Milling, 1986; 2002). The links between the range of mathematical formulations, stock/flow representations and different applications of the diffusion concept are described by Lane and Husemann (2004), as is their usage in sociology (Coleman, Katz, & Merzel, 1957; 1963) and origin in the work of Verhulst (1838).

2.3. The FSA's role

The modelling work described here resulted from a 'call' by the Food Standards Agency, or 'FSA'. The FSA is a non-ministerial department of the UK government. Created in 2000 by the Food Standards Act of 1999, its stated objective is; "…to protect public health from risks which may arise in connection with the consumption of food (including risks caused by the way in which it is produced or supplied) and otherwise to protect the interests of consumers in relation to food" (Food Standards Act 1999; Section 1 (2)). Its remit regarding food safety and hygiene includes research, consumer advice and legislative recommendations relating to the growing, handling, packing and preparing of food.

The work was part of the broader aspiration to, "reduce foodborne disease using a targeted approach", an established FSA Strategic Objective (Food Standards Agency, 2011, p. 1). With NV being one of the most common sources of foodborne disease in the UK, there was a perceived need to understand the extent to which foodborne effects influence transmission and so begin to probe how the operation of those FB transmission mechanisms influences the scale of NV outbreaks. However, the situation is complicated by the fact that, unlike pathogens such as *Salmonella* or *E. coli* O157, NV does not grow within foods, nor does it originate in them. Instead, as described in Section 3, via a number of mechanisms, infected humans can infect certain foods which are then vectors, generating further transmission. To understand the significance of FB transmission it was therefore necessary to grasp the interplay between this range of transmission routes and the more common P2P transmission.

This was the context in which the FSA commissioned research via a 'call': 'Request for Quotation – System Dynamics Model for Norovirus'. Its primary aim was to support the development of a simulation model, that is, to conceptualise, formulate and parameterise a model which included both P2P effects and primary FB infection mechanisms. Doubts were expressed from the very start by FSA staff: there was a view that, given current knowledge, it would be hard to construct such a model and very likely impossible completely to parameterise it. Nevertheless, it was envisaged that modelling would help inform the FSA's strategy for tackling NV in four ways. First, by supporting an assessment of how reducing risks in the food chain might have an effect on human cases. Second, by allowing the development of a better understanding of the relative contributions of the food-related routes of

transmission. Third, by facilitating an assessment of where risk reduction might be most beneficial. Last, by identifying gaps where further work may be required.

The subsequent work actually used two different approaches – described in the following two sections.

3. Endogenising the foodborne mechanisms

This section describes the process and content of the work done directly for the FSA: the creation and use of a large simulation model 'FSA NoV Model' via the System Dynamics approach (Forrester, 1961; 1968).

3.1. Extending an existing modelling

The P2P sector of our model built on a previous study (Lawrence, Kerrod, & Gani, 2004). They employed a variation of the standard formulations discussed in Section 2.2. We made some extensions to produce the following ordinary differential equations (ODEs):

$$\frac{dS}{dt} = -\left(\frac{\beta I}{N} + \theta\right)S + \delta R + \mu(N[1-\chi] - S)$$

$$\frac{dE}{dt} = \left(\frac{\beta I}{N} + \theta\right)S - (\mu + \alpha)E$$

$$\frac{dIs}{dt} = \alpha(1-\kappa)E - (\gamma + \mu)Is$$

$$\frac{dIa}{dt} = \alpha\kappa E - (\gamma + \mu)Ia$$

$$\frac{dR}{dt} = \gamma(Ia + Is) - (\mu + \delta)R$$

$$I = Is + \omega Ia$$

As the FSA requested, our model used Vensim (Eberlein & Peterson, 1992; Eberlein, Melhuish, & Peterson, 1991). We therefore explain the P2P sector using a stock/flow diagram (Lane, 2008) and ODEs, employing both the long variable names typical of System Dynamics work and Lawrence et al.'s algebraic terms (see Fig. 2).

Births and deaths use a dwell time parameter 'Life Expectancy' (in Fig. 2); the reciprocal of this parameter being μ (in the ODEs). These balance out, giving a constant 'Population Size N'. Those 'Permanently Protected' lack the receptors that respond to NV but remain in the mixing population. Their proportion is the parameter 'Proportion of Pop Non Susceptible to NV Chi', or χ.

The remainder of the population plays a range of roles and is treated using five state variables, or stocks. The 'Susceptible Individuals', or S, can be infected by NV, becoming 'Exposed Individuals', or E, people hosting NV who are not yet infectious. The average time in this category is the 'Latent Period'; α is the reciprocal. After this time members of one group, 'Infectious Symptomatics *Is*', develop symptoms and become infectious because they shed the virus. However, experiencing infection as an illness does not occur in all cases. Instead, a proportion of the exposed – given by the parameter 'Asymptomatic Carriage Proportion', κ – become 'Infectious Asymptomatic *Ia*' (Lindesmith, Moe, & Marionneau, 2003; Tompkins, Hudson, & Smith, 1999). These are Norovirus-carrying individuals who show no symptoms but may still shed the virus.

The period individuals dwell in either infectious stock varies considerably (Milbraith, Spicknall, & Zelner, 2013). Here an average duration is used, 'Infectious Period'; γ is its reciprocal. Infectious individuals become 'Recovered Immune', R. They no longer shed the virus but have acquired immunity which wains after an average time – 'Period of Immunity'; δ is the reciprocal. Estimates for this parameter also vary (Greenberg & Matsui, 1992; Johnson, Mathewson, & DuPont, 1990; Simmons, Gambhir, & Leon, 2013). These individuals cycle back to being susceptible.

Exposure to NV originally had two elements. The P2P mechanism is the central concern of this sector. Homogenously mixing susceptibles are exposed for a range of reasons: viral shedding occurring prior to obvious symptoms from infected individuals still in a social setting; illness being so rapid in onset that individuals vomit or defecate in shared spaces; healthy individuals being involved in caring for someone with the illness; infectious individuals returning to social settings before complete recovery. These combine into the 'Exposure Rate' using a standard epidemiological formulation, $\beta I/N$. The parameter 'Beta' is the number of social 'encounters' per day that each susceptible engages in which can result in exposure if an infectious person is encountered. The probability of a susceptible encountering an infective person within the mixing population is included via the formulation I/N. As shown in the equations, the term I sums the two infectious stocks. However, as an extension to previous work there is now a parameter 'Weighting for Infectious Asymptomatics', ω. This expresses the fact that the extent to which asymptomatics are infectious is not well known, an idea discussed further in Section 4.1.

A second element of the exposure rate is also shown here – but only prior to its complete removal and replacement. In the Lawrence et al. model the FB effects were represented via the forcing term 'Theta', θ. This parameter is the proportion of susceptibles exposed per time period as a result of FB effects. This is an exogenous formulation, retained in the equations above to illustrate the approach of past research. The core aim of our study was to replace this with an entirely endogenous treatment of the FB effects. In other words, to replace θ with the mechanisms underlying FB infection. The means of doing this is presented in the next two sub-sections, in terms of process and then content.

3.2. Model development process

Our central aim was to elicit information, represent it in a model, encourage critical comment on the assumptions and so improve the quality of the model. The general idea is now well-established in OR (Bryson, Ackermann, & Eden, 2004; Franco & Montibeller, 2010; Rosenhead, 1989). In our work a combination of approaches was used – something known to be effective (van de Ven & Delbeco, 1974) – and an iterative mixing of literature review, individual expert interviews and facilitated 'group model building' brought to bear.

A literature review allowed the Operational Researchers to develop a basic understanding of the area, create initial, 'candidate' elements of a model, and plan a detailed process for the study. The FSA then arranged access to highly experienced and informed individuals from the areas relating to FB transmission. With them we used individual interviews to create a System Dynamics model (Lane, Monefeldt, & Husemann, 2003; Vennix & Gubbels, 1992). The FSA established strong links with staff from: Animal Health & Veterinary Laboratories Agency (AHVLA), Centre for Environment, Fisheries & Aquaculture Science (CEFAS), Food & Environment Research Agency (FERA) and Public Health England (PHE). Further experts from the FSA itself were consulted. Engagement with each expert followed the same pattern. There was one or more 'non-modelling' session – interviews conducted by phone or face-to-face, guided by an agenda informed by the literature review. The resulting information was then represented using System Dynamics software. As necessary, the literature was consulted further to clarify points or to gain a grounding in new areas that the interviewees had introduced. The experts were then sent a note on stock/flow diagramming containing examples of the symbols. They

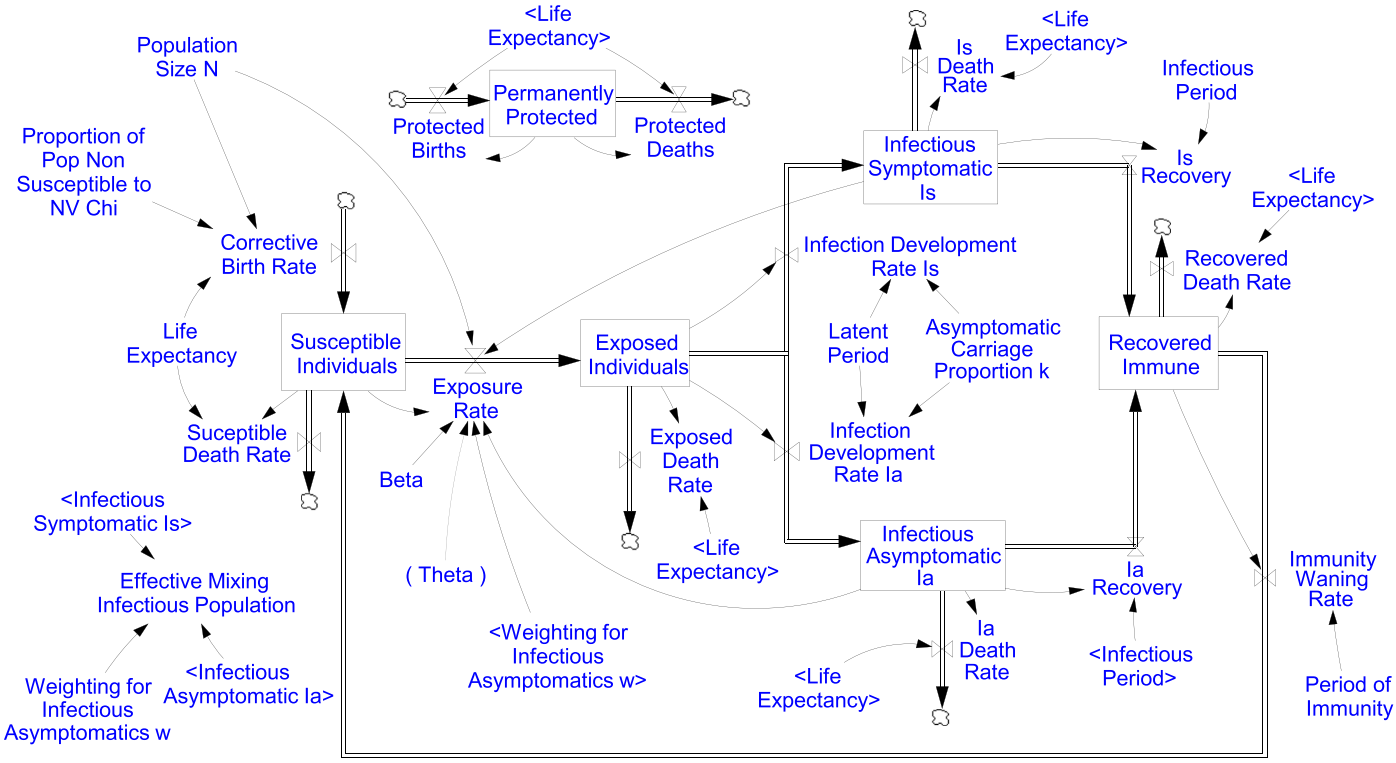

Fig. 2. Stock/flow diagram illustrating the person-to-person sector of the 'FSA NoV Model'. Bracketed variables – <Name> – have values calculated elsewhere in the model.

also received a copy of the stock/flow diagram of the P2P sector, and a diagram of the specific model sector on which they were being consulted. This was followed by one or more further interviews, the discussion shaped by the model itself and using the language and iconography of System Dynamics modelling. The aim was to make each expert satisfied that the part of the model they worked on represented their understanding of the mechanisms.

Considerable amounts of modelling took place outside the interviews; representing what had been read, unearthing further questions intended to elicit knowledge, representing new information that was elicited.

The final stage was a 'group decision support' session. Such facilitated sessions are a recognised way of actively engaging stakeholders in developing some form of model. They may involve a number of OR tools specifically designed to be used in a facilitative manner (Eden, 1992; Eden & Radford, 1990; Franco, 2013; McCartt & Rohrbaugh, 1989; Phillips, 1989), though the idea is also spreading into traditional simulation modelling (Edwards, Alifantis, & Hurrion, 2004; Robinson, 2001; Robinson, Worthington, & Burgess, 2014; Tako & Kotiadis, 2015) . In System Dynamics terms, this participative approach is part of the defining ideas of the field (Forrester, 1971; Lane, 2010), increasingly used in practice in recent decades (Vennix, Andersen, & Richardson, 1992; Vennix, Gubbels, & Post, 1990), and underpinning 'group model building' (Lane, 1992; Richmond, 1997; Vennix, 1996).

For this work we organised a facilitated workshop at the FSA's London offices. It brought together all the experts and, in a carefully structured collaborative session, exposed each sector of the model to comment from all participants. The process was designed to ensure that all participants were engaged and every part of the model was brought into the discussion, in terms of both specific, unresolved questions and the wish to draw the group into becoming 'owners' of the model. The meeting room had large printouts of the model attached to its walls (see Fig. 3). This allowed a peripatetic element: the hours spent working were punctuated by periods in which all participants stood and assembled around each of these print-outs, and offered comment – even annotating the stock/flow diagrams by hand. Moreover, this room layout meant that beyond what was projected onto a central screen, any participant could check again on any structural assumption of the model simply by looking around the room to the relevant section map. The session also gave the authors an opportunity to discuss a list of algebraic formulations which they particularly wanted to invite comment on, and to ensure that the model was richly documented, this being done 'live' using a projected version of the Vensim model.

After this meeting the participants' corrections, clarifications and additional comments were transferred from meeting notes and sketched-on diagram changes into the model itself. The model thus became, in the opinion of those present, a sensible and plausible shared account of the mechanisms underlying FB transmission, couched in meaningful, conceptually plausible variables.

Methodologically, by demonstrating the effectiveness of a combination of individual sessions with domain experts and a facilitated group modelling session, the approach is consistent with the idea that direct, collaborative participation in model building is important to creating the 'buy-in' of stakeholders and also relates the study to continuing discussions about the effectiveness of facilitated approaches (de Gooyert, Rouwette, & van Kranenburg, 2017; Franco & Greiffenhagen, 2018; Scott, Cavana, & Cameron, 2016). Moreover, the sequence and range of different approaches employed fits with the rejection of the idea that 'validity' is like a one-time inoculation (Richardson & Pugh, 1981). Instead, 'confidence' arises via activities undertaken over a period. This idea appeared some time ago in the literature (Forrester & Senge, 1980; Gass, 1983; Greenberger, Crenson, & Crissey, 1976) but is now found in UK government guidelines (HM Treasury, 2015; NAO, 2016). For example, one element of this approach is the gradual process of building up 'face validity'. A comment on the creation of another System Dynamics model – "… every stage of the model development was discussed with people who understand the system and so the model's face validity was considered to be

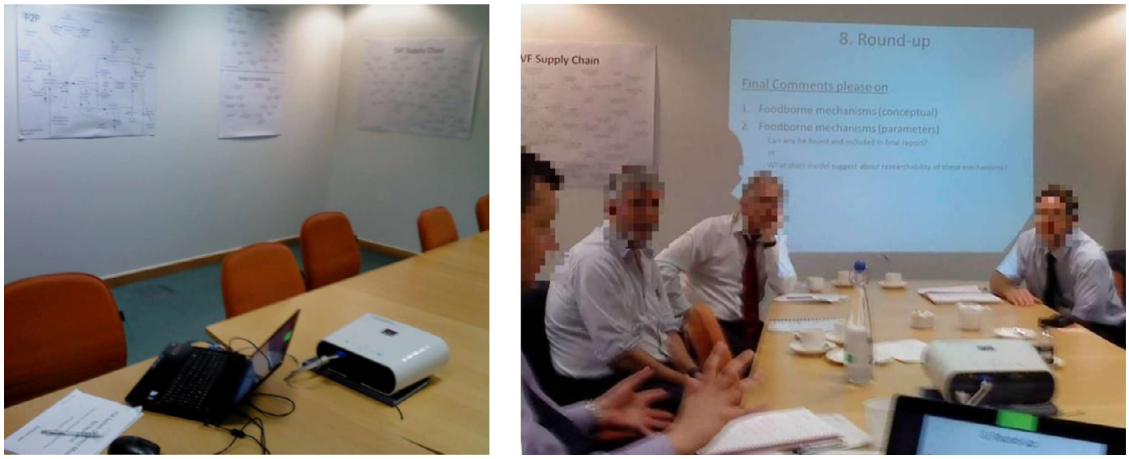

Fig. 3. Scenes from the workshop at the FSA. Left: room layout showing the large posters of the model's sectors. Right: expert participants discuss the model.

extremely high" (Brailsford & De Silva, 2015, p. 1571) – applies to this work too.

3.3. Structure of the extended model

Our 'FSA NoV Model' has almost 150 variables, 14 being stocks. Each variable within the model is documented: its underlying ideas, which experts it had been discussed with, and relevant research citations. Further, detailed information about the model is available via the FSA website: https://www.food.gov.uk/research/foodborne-diseases/modelling-the-foodborne-transmission-mechanisms-for-norovirus. For the purposes of this paper, for each of the model's four FB sectors, we outline the mechanisms in operation and their representation.

The first sector concerns sewage contamination of bi-valve shellfish such as oysters. Infectious humans excrete NV genomes. Before being discharged into the ocean, sewage is treated via percolation and by UV lights, reducing the presence of NV. Nevertheless, some genomes still flow into estuary farm areas, where they otherwise dissipate over time. However, bivalve shellfish filter sea water in order to feed and so absorb genomes (Lowther, Gustar, & Hartnell, 2012). After harvesting, shellfish are cleaned, again reducing the genome presence. Humans eat shellfish (often raw or undercooked) which can lead to infections (Lees, 2000; Smith, 2018).

The model treats these effects as follows. The input from the P2P sector is *I*, the weighted sum of the two infectious stocks, given the name 'Effective Mixing Infectious Population' (see Fig. 4). The model treats the situation as two conserved subsystems (Richardson & Pugh, 1981): two stocks model the genomes in farm areas, some absorbed into shellfish, some not; a single stock represents the shellfish. Genomes are absorbed into the bodies of farmed shellfish. This co-flow structure calculates the number of genomes in harvested shellfish. Relating this to the presence of susceptible humans produces the key output, the variable 'Infections per Day from Shellfish'.

The second sector concerns 'Sludge Contamination'. Again, NV genomes pass into sewage, some of which is used to create sludge, a fertiliser applied to soil. NV presence is diluted via a complex process. First, particulate sludge is separated from the effluent element of sewage. Then a feed of bacteria is applied which anaerobically digest solids, breaking down molecules - this is called mesophilic anaerobic digestion. Both processes reduce NV presence by orders of magnitude (Gale, 2003; 2005). The use of sludge is carefully controlled (ADAS Safe Sludge Matrix, 2001; DEFRA, 2015); for some crops, treated sludge is applied to top soil. Any remaining NV slowly decays but when food is harvested, even after washing, it may still have soil and hence NV adhering to it. Hence there is a possibility of human transmission.

The focus in this sector is on cultivated foodstuffs eaten uncooked as these are more likely to convey NV. This sector therefore concentrates on soft fruits (including berries), salad ingredients and vegetables eaten raw. The summarising term 'BFLV' – berry fruits and leafy vegetables – was created to refer to these.

The model treats the above effects as a causal cascade in which a range of processes dilute the presence of NV. It generates a measure of NV presence in an average BFLV portion and that yields this sector's output; 'Probability of BFLV Food Portion Contamination Via Sludge Contamination'. This is used in the next sector.

The third, and most complex, sector of the model concerns the BFLVs supply chain. Contamination may occur at any of three stages. The first stage is harvesting. As described, food grown on sludge-fertilised land can retain some NV. Additionally, all BFLVs may be harvested by workers who themselves transfer NV, perhaps because they are infectious, possibly made worse by poor toilet and hand washing facilities on some farms. Second, such foods can be contaminated at the 'processing' stage, for example when a lettuce is being washed and wrapped, or when spring onions are bundled together for sale. Finally, BVLF can become contaminated by human contact at the point of preparation and consumption, in a home kitchen, or in a catered setting such as a restaurant, fast-food outlet or staff canteen. Todd, Greig, and Bartleson (2009) describe the role of viral transmission in such processes.

This rich set of ideas was implemented using the stocks and flows shown in Fig. 5. The complexity of the model derives from our including the variables that influence these flows, linking these to inputs from the P2P sector, or the sludge sector, providing relevant intermediate parameters/variables, and including the processing rates and dwell times of the supply chain stages and activities. Such granularity was thought vital. For example, catered food preparers contract NV in the same manner as others but may have different behaviour regarding withdrawing from work if feeling ill, or give a different amount of attention to hygiene whilst working. Similarly, home and catered use were treated separately. Here 'home' implies situations where food is handled by someone who themselves eats it, or who eats other food from the same preparation area. The parameters are different because, unlike catering establishments, home activity is not subject to legislation or hygiene inspection: only advice and education can alter behaviour. In this way the sector generates outputs that loops back into the P2P sector: 'Infection Rate per Day from Home Prepared BFLV food' and 'Infection Rate per Day from Catered BFLV food'.

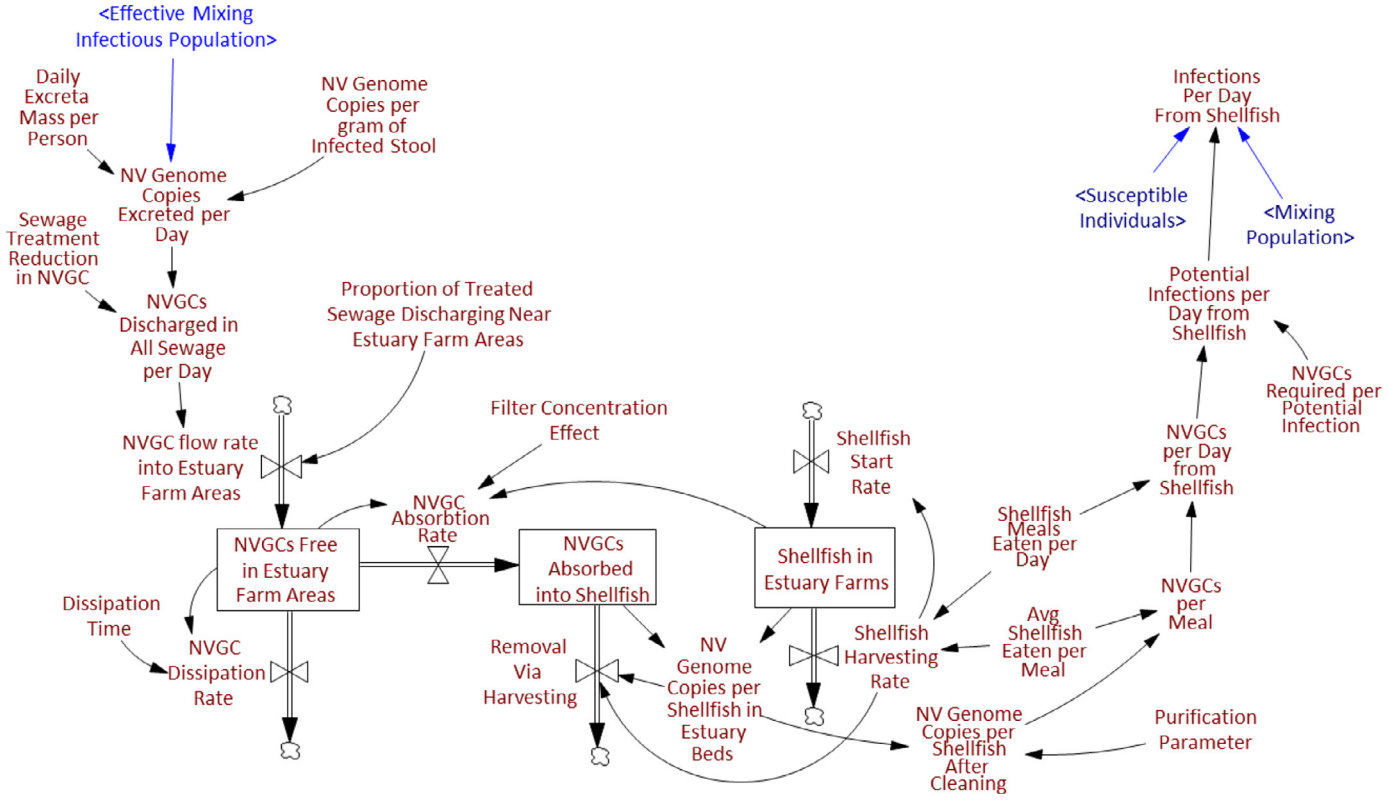

Fig. 4. Stock/flow diagram of the 'Bivalve Shellfish' sector of the 'FSA NoV Model', showing the people-to-shellfish and shellfish-to-people transmission mechanisms.

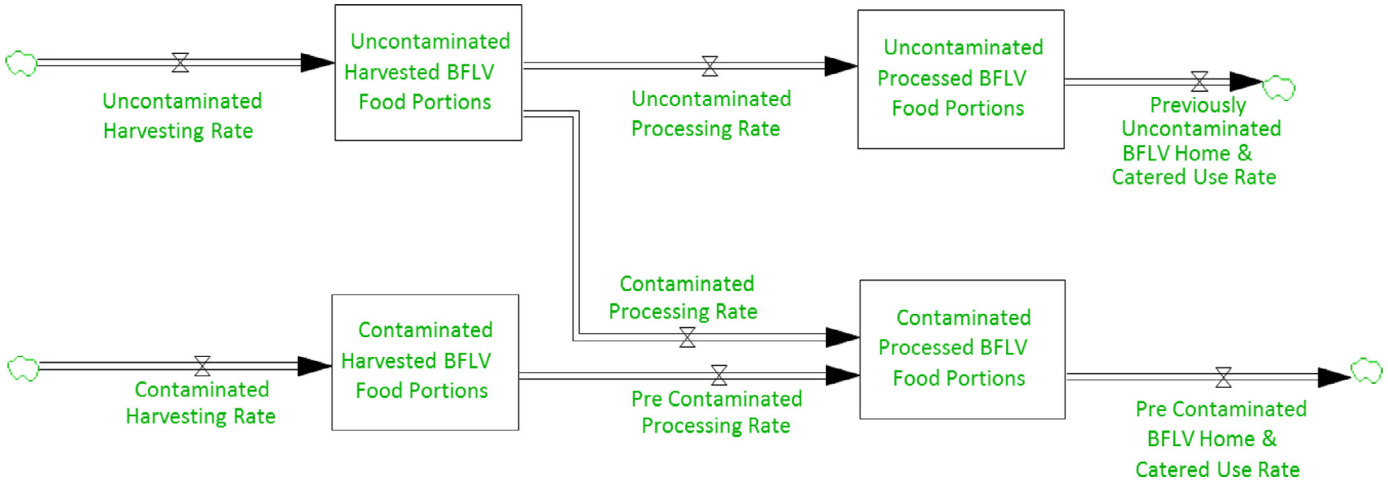

Fig. 5. The 'BFLV Supply Chain' sector of the model, showing only the stock and flow rate variables.

The final FB-related sector concerns other foodstuffs. It deals with the 'use' phase, again handling home and catered use separately. The idea is that previously uncontaminated food may still acquire sufficient NV genomes to effect transmission; Wilson (2016) gives a vivid description of the everyday realities.

This sector has a high conceptual complexity, similar to that of the previous one. From the state variables in the P2P sector it calculates the proportion of food caterers and home preparers who are infectious and treats the number of food portions produced per day and the availability of susceptible diners. It generates output 'Infection Rate per Day from Home Prepared All Other Food' and 'Infection Rate per Day from Catered All Other food' and these close the feedback loops by passing back into the P2P sector.

3.4. Contributions of the endogenised model

The new model has five sectors, four dealing with FB effects and the P2P sector which is now amended to also bind together the elements from the other four. The exogenous term Theta is removed, replaced by complex causal chains representing the FB infection mechanisms in an endogenous manner. The contribution of this model has two parts.

The first contribution is the model's existence. The model has assumptions and literature sources carefully documented within it. It is transparent and comprehensible. Therefore, the model demonstrates something about which the FSA was by no means certain: that enough is known about the FB mechanism to create a sound

Table 1
A 2×2 organising framework for the parameters in the 'FSA NoV Model'. This assisted the creation of a research agenda and allowed the identification of potential policy levers.

	Fixed	Alterable
Known Value	Fixed, Known	Alterable, Known
Unknown but Researchable Value	Fixed, Unknown	Alterable, Unknown

model that specialists in the area – not just operational researchers – understand and accept as such.

The work was subject to an FSA peer review which supported this point. It described the model as, "well-documented … demonstrates good practice … impressive" and stated that it, "has made a substantial contribution to discriminating between foodborne and person-to-person infection routes" and "improves the understanding of mechanisms."

The model captures the current state of thinking across a range of specialisms and contributes to the Norovirus literature. It is a vehicle for the sharing of that thinking amongst researchers who concentrate on one aspect of NV but are also interested in the broader consequences of NV cases – it facilitates that 'out of the silo thinking'. It is an agreed representation of our best understanding of NV transmission. Useful for all of these reasons, the model itself is a key contribution of the study.

The model is fully conceptualised, completely formulated, its relationships dimensionally consistent, all of its parameters meaningful and measurable. Nevertheless, it was possible to parametrise the model only partially. Naturally, every attempt was made to address this. The research literature was comprehensively used. Consulting experts to establish the assumptions in a model (including parameter values) is standard for System Dynamics (Forrester, 1961; Graham, 1980; Vennix et al., 1992) and this was extensively used.

The partial parameterisation was not a concern for the FSA. Indeed, it was no surprise since staff had believed from the start that current knowledge of NV was incomplete. In fact, the modelling work made more progress than had been expected - a return to the study's first contribution.

This qualification aside, there was a second contribution. Exactly because of the model detail and its careful conceptualisation, formulation, and dimension checking, it was possible to think about the parameters in two new ways.

An initiating idea came from a workshop participant: that the model could help clarify what was still unknown about NV. This thought was immediately supported by the others present. Subsequently, another dimension was added to this idea. As a result, for each of the model's parameters, two questions were asked: Do we know the parameter value or do we need more research? Is the value fixed by nature or could human behaviour alter its current value? In this way all of the model's many parameters were categorised using a 2×2 framework (see Table 1).

This approach helped in two ways. First, it helped the FSA think about where the gaps were in current knowledge, what it was still necessary to research and find out. This was useful in contributing to agenda-setting for future research. Second, parameters that can in principle be altered are potential 'policy parameters' (Richardson & Pugh, 1981). Hence, using examples from Fig. 4, the 'Daily Excreta Mass per Person' is known and fixed, whilst the 'Sewage Treatment Reduction in NVGC' is known but in principle alterable. Finding these was useful for beginning to identify leverage points relating to NV.

This approach was strongly aligned with the four ways that the FSA had hoped the study could contribute to its strategy for NV risk reduction (see Section 2.3). Additionally, the FSA review found that, "For the scientific community … [it] helps to direct research effort" and "informed possible food chain interventions."

To repeat, the original insight that the model could be useful in this way came from workshop participants who had spent time creating and understanding the model and so were able to grasp its potential and use it in a creative manner.

4. Scoping the foodborne effects

The work discussed above was what the FSA expected of the study, a satisfactory response to the original call. However, the unearthing of some new data and the application of creative thinking made it possible to take things in an unexpected direction. The resulting modelling appreciably extended the work – and is the subject of this section. It contributed significantly to the FSA's aims by, for the first time, allowing for a quantitative analysis of the scope of P2P and FB effects.

4.1. Calibrating a compact model

The first step was the identification of new estimates of three parameters. The first was the 'Asymptomatic Carriage Proportion', or κ, the proportion of those exposed to NV showing no symptoms but still shedding the virus. Lawrence et al. (2004) used the value 0.003. Further discussion with FSA staff took place, including important clarifications amongst them regarding the range of definitions used in the literature. Eventually a new value of 0.12 from Phillips, Tam, and Rodrigues (2010) was agreed to be a better estimate. (This discussion was used as an exemplar of ensuring 'data validity' in a model, see Government Office for Science, 2018).

It was this significant increase in value that motivated us to introduce into the equations shown in Section 3.1 a new parameter for the differential infectivity of asymptomatic infective individuals. This 'Weighting for Infectious Asymptomatics', ω, expresses the fact that the infectiousness of asymptomatic viral shedders is not well known. There are two reasons for this (Amar et al., 2007; Bull, Eden, & Luciani, 2012). First, whilst some asymptomatic individuals shed particles of NV not all do, and they do so to different extents than symptomatics. For example, whilst 16% of adult asymptomatics shed NV, the percentage is greater for children, possibly rising to ~30% for those below 12 months. Second, asymptomatic adults are more mobile, exhibiting a higher social mixing rate than symptomatics exactly because they experience no debilitating symptoms and are unaware they are infected. This uncertainty might have seemed less important when only 0.3% of those exposed became asymptomatic but 12% must give pause for thought. Including ω provided a simple platform for this uncertainty, given the evolving knowledge in this area.

Two further parameter values resulted from a large scale study (O'Brien, Larose, & Adak, 2016; Tam et al., 2012). The first was

Table 2
Inputs to the extended P2P model. The time period is [days].

Model parameter	Value	Symbol
Population size	61,792,000	N
Asymptomatic carriage proportion	0.12	κ
Weighting for infectious asymptomatics	1	ω
Proportion of pop non susceptible to NV Chi	0.2	χ
1/Latent period	0.5	α
1/Infectious period	0.5	γ
1/Period of immunity	2/365	δ
1/Life expectancy	$1/(78 \times 365)$	μ
Observed incidence rate	7960	Φ
Foodborne proportion of incidence rate	0.02527	π

Table 3
Outputs of the base case steady state calculations with the extended P2P model: NV prevalence and infection parameters. The time period is [days].

Steady state values derived from model	Value	Symbol
Footprint:		
Susceptible individuals	47,757,000	$\bar{S}$
Exposed individuals	18,090	$\bar{E}$
Infectious symptomatic *Is*	15,918	$\overline{Is}$
Infectious asymptomatic *Ia*	2170	$\overline{Ia}$
Recovered immune	1,640,100	$\bar{R}$
Infection effects:		
Forcing term for the foodborne effect	4.7866×10^{-6}	θ_0
Person-to-person infectivity	0.63068	β_0

an annual NV incidence rate of 2,905,278 (95% CI: 2,418,208–3,490,451) – down from the estimate of 3.7 million in Tompkins et al. (1999). This value becomes 7960/day and will be referred to as the 'Observed Incidence Rate'. In model terms it equates to the variable 'Infection Development Rate Is' (see Fig. 2) and the symbol Φ is used for it.

The second value concerned cases attributable to FB mechanisms: a 95% 'credible interval' of 50,320 – 104,000 cases per year, best estimate 73,420. At the study's start the cautiously held view for the fraction of FB cases was 0.107 (Adak, Long, & O'Brien, 2002). The calculated value is now sharply reduced: 0.02527. This proportion will be referred to as the 'Foodborne Proportion of Incidence Rate' and the symbol π used.

These three additional values made it possible completely to calibrate the extended P2P model. The equations in Section 3.1 and the parameters in Table 2 were used. Setting the differentials to zero gives equations for the steady state values – standard notation $\bar{X}$. Two further equations follow:

$$\Phi = \alpha(1-\kappa)\bar{E}$$

$$\theta = \left(\frac{\pi}{1-\pi}\right)\frac{\beta}{N}\left(\overline{Is} + \omega\overline{Ia}\right)$$

It is then possible to find analytical solutions for this set of equations. The mathematics is straightforward – though care is needed – but the result is very useful. Shown in Table 3, one deduces the prevalence or 'footprint' of NV (the number of individuals in each of the stocks shown in Fig. 2), as well as estimates for the P2P effect, β, and the simple representation of the FB effect, θ. These results are the very first empirically-grounded calibration of a P2P model for NV.

4.2. Understanding model sensitivity

The above calibration is the Base Case, the 'As Is World': parameter values including the observed NV incidence rate and FB percentage are 'processed' via the assumptions and logic of our extended P2P model to produce estimates of θ and β operating in the world – θ_0 and β_0.

It is possible to reverse this analysis to create a 'What If World'. Now Φ and π are unknowns. Instead, the other parameters, combined with exploratory values of θ and β, are 'processed' through the model's assumptions. Again, the mathematics is straightforward – though involving even more tedious algebra. Nevertheless, it is again possible to produce analytical solutions of the steady state equations. What results is expressions for: NV prevalence, NV incidence rate and FB percentage in scenarios with different assumed values of θ and β. This approach allows model sensitivity to be explored in a way which directly addresses the FSA's aims for the study. It gives a quantitative 'scoping' of the relative importance of P2P and FB effects. This analysis has two parts.

First, it becomes possible to examine the sensitivity of the model to θ, the first-cut representation of FB transmission. The 'What If World' approach is used repeatedly, the results best considered using a spiderplot (Eschenbach, 1992). Fig. 6 shows values of annual NV incidence rate in millions of cases plotted against the proportional value of θ used in each exploration. It follows that $X=1$ represents the 'As Is World'. The uppermost line is the 'Observed Incidence Rate' and it passes through (1, 2.905278), reproducing the Base Case. This output is disaggregated into infections from P2P and FB effects. The lowermost plot – the FB infections – makes up only 2½%, correctly reproducing the Base Case value of π.

The non-linear response is noteworthy. If θ is doubled then total NV incidence increases by about 33%. However, if θ falls to zero incidence collapses by 75%. Moreover, simulation with θ arbitrarily reduced to zero shows that that plunge in incidence to only 25% its Base Case value occurs in only about a year of simulated time (this response time can be seen in the model runs of Fig. 9). This counter-intuitive response reveals that FB infections have a very powerful 'forcing effect' on the system, lifting overall incidence to much higher levels.

This response indicates that the figure of 2½ % for FB cases is misleading: in dynamic terms θ is playing an important role, producing a significant threshold effect. With so much to gain from changing θ (and, potentially, in a timeframe of just a year) it seems quite correct of the FSA to look into ways of reducing FB transmission effects.

The second part of this analysis yields an equivalent spiderplot showing the effect of experimenting with P2P effects via β (See Fig. 7, top). With P2P infections making up 97½% of infections in the Base Case the collapse when $\beta=0$ is unsurprising. However, as discussed further in Section 4.3, significant reduction actually occurs much earlier than that. Viewing the response in logarithmic terms (Fig. 7, bottom) it can be seen that a mere 25% reduction in β causes an order of magnitude change in incidence. However, the vertical scale in Fig 7, top shows the remarkable response to a doubling of β: at 43 million, incidence is 15 times the Base Case value.

Two insights flow from this sensitivity analysis and these are discussed in the next two sub-sections.

4.3. Insight I: seasonality

Sensitivity analysis offers a possible explanation for seasonal variation in NV incidence. Data for the Winter of 2016/17 was shown in Fig. 1. That variation is not an anomaly (see Fig. 8). Despite shifts in phase and severity, the qualitative pattern holds: Winter incidence is roughly ten times greater than its Summer value.

There are certainly exogenous seasonal effects driving the system: for example, farming has harvesting seasons and this variation will be drawn into system via the FB effects; lower temper-

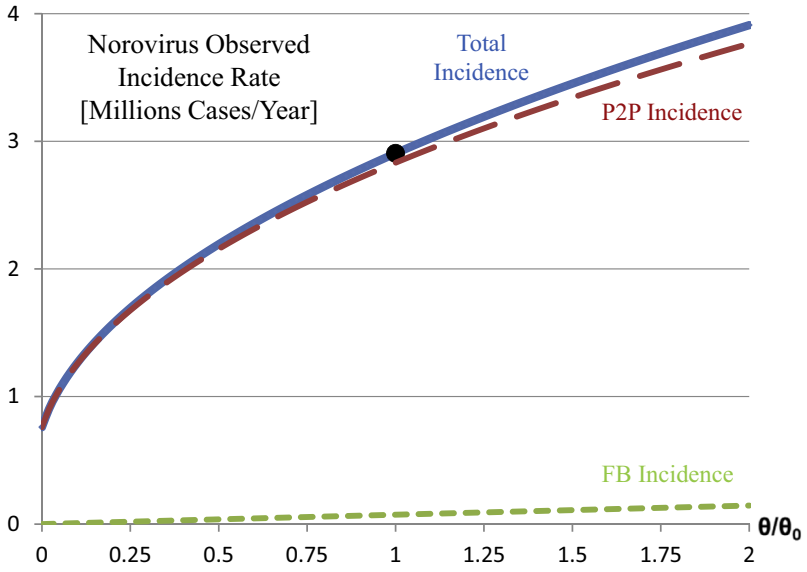

Fig. 6. Spiderplot of annual incidence rates against the relative size of the FB effect, θ.

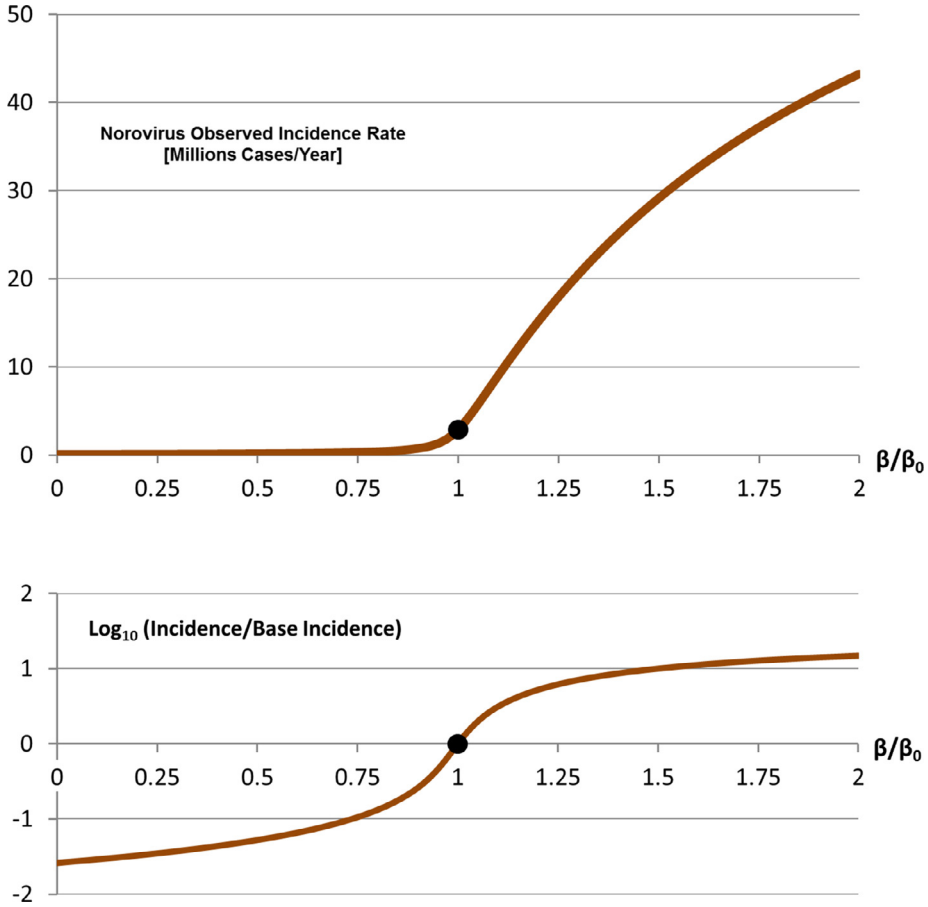

Fig. 7. Annual Norovirus incidence against the relative size of the P2P effect, β. Top: spiderplot of actual incidence rate. Bottom: spiderplot of relative incidence, also against relative value of β but with logarithmic vertical scale.

atures and sunlight levels in winter may allow NV to survive for longer on surfaces. However, we choose to focus on the P2P aspects of infection, to explore whether they alone might offer an explanation. Clearly human behaviour relating to NV does change across the seasons: in lower temperatures people stay indoors more and are in closer proximity; they are more likely to suffer colds, creating additional aerosol transmission. However, it is hard to imagine those effects as being as large as an order of magnitude. The question we therefore chose to explore is: Can changes in human behaviour alone possibly be the source of the marked seasonality?

One line of thinking involves returning to the β sensitivity of Fig. 7. Consider the point (1, 2.9). The curve here is highly non-linear. A decrease in β by 25% reduces incidence to barely 11% its

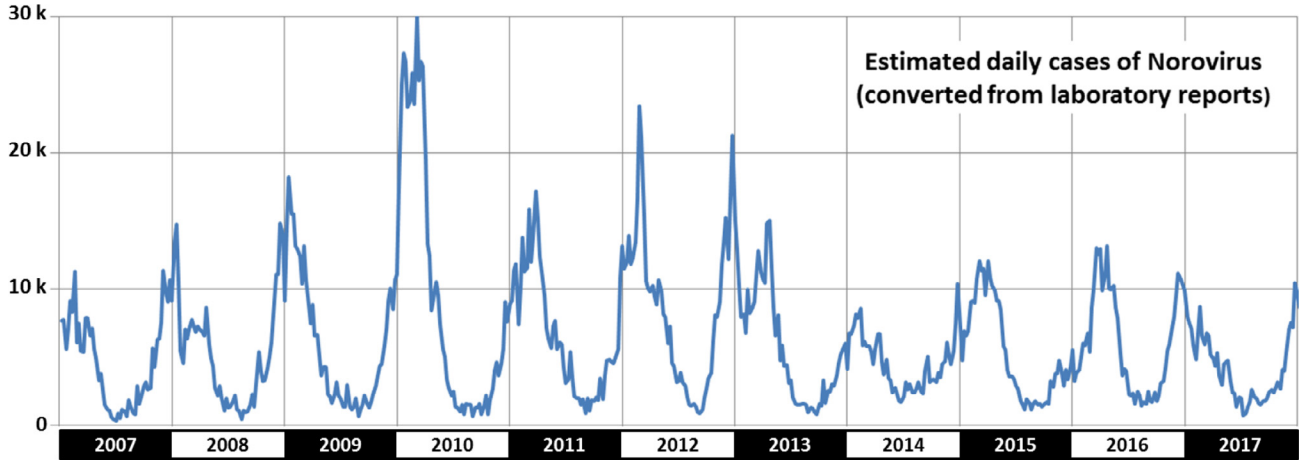

Fig. 8. Estimated Norovirus incidence data in England and Wales for 2007–2017. Some of the data is provisional at the time of writing. Data source: Public Health England.

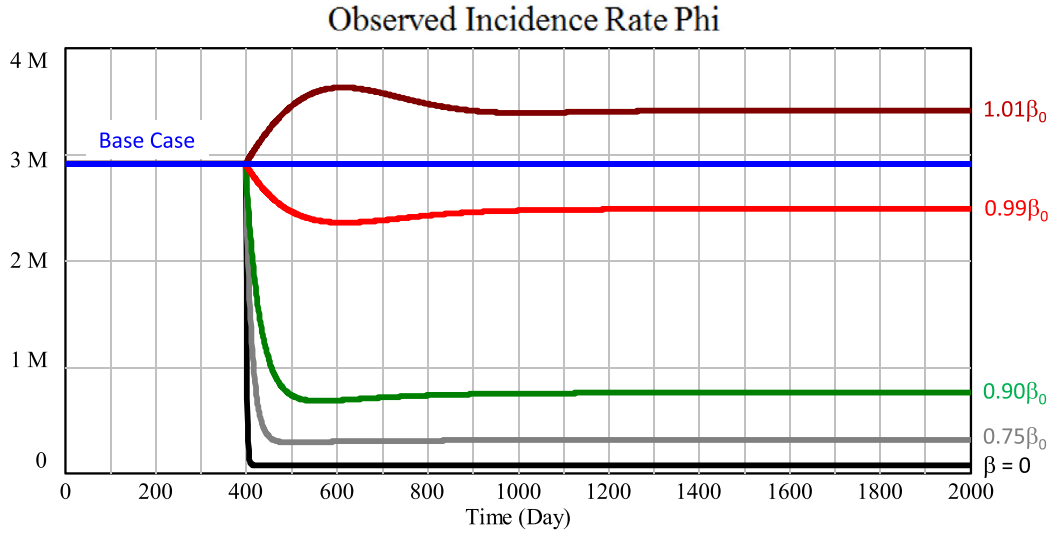

Fig. 9. Simulations of the extended model showing the effect of varying P2P infectivity. Note the general response time of about a year.

base value. Indeed, so non-linear is the relationship that decreasing β by 1% decreases incidence by 15%, whilst a 1% increases in β increases incidence by 17%. These sensitivities are all confirmed by the simulations of the model shown in Fig. 9. These suggest that quite small seasonal variations in β might be behind the data of Fig. 8.

This idea progresses in two steps. First, from the empirical data we can extract an averaged-out multiplicative seasonality effect (Kendall, 1973). This is shown in Fig. 10 as the chain line. Around the average of one, this curve has a low of around $^1/_5$ and a high at $2^1/_3$. This captures the order of magnitude difference in peak-to-trough behaviour seen in the empirical data. Using the 'What If World' analysis, this seasonality multiplier can be converted into time-varying, instantaneously consistent values for β. At this point, the strong sensitivity to β of NV incidence means that a consistent β multiplier – or β/β_0 term– has much lower variation. Shown in Fig. 10 as the solid line around an average of 1, it has a low of 0.86 and a high of only 1.06.

The second step adds a random element. There is a range of possibilities (Leemis, 2004). Because aggregate human behaviour is seldom wholly random and capricious we used a 'pink noise' formulation: uniformly distributed, uncorrelated white noise was passed through a first-order exponential smoothing formulation to produce an auto-correlated and asymptotically Normal series with mean zero. The resulting values of β are shown in Fig. 11, top.

Applying this formulation to the model generates the data shown in Fig. 11, bottom. This simulated data can then be compared with the actual data of Fig. 8. The fit is not perfect – it avoids the wilder excursions and there is some phase variation. Nevertheless, it does offer a possible answer to our seasonality question. Variations in human behaviour need not themselves be large: our seasonality multiplier peaks at +6% of base value β_0 and bottoms out at −14%, whilst the pink noise adds ~±3% to this. This is all that is needed in human behavioural terms. Can, then, changes in human behaviour alone possibly be the source of the marked seasonality? Yes: human behaviour changes of an entirely plausible scale, combined with the sensitivity of the current system to changes in P2P effects, may be a significant component of the strong seasonality of NV incidence.

4.4. Insight II: policy focus

The second insight concerns the relative importance of FB and P2P effects.

In Fig. 6, to the right of the $X=1$ point ($\theta=\theta_0$), the reduction from $X=2$ indicates the scale of the benefits already achieved via existing food production and hygiene legislation and guidelines. Moving into $\theta<\theta_0$ then indicates the scale of potential benefits that might still be gained. Clearly the 'FB front' is worth exploring.

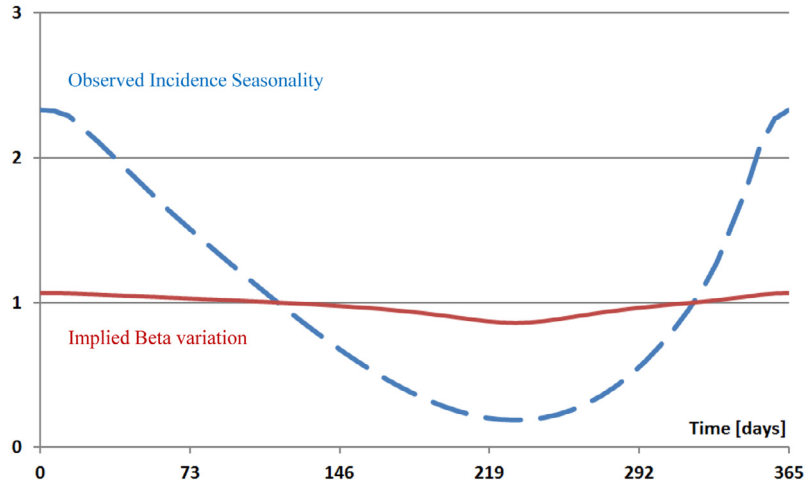

Fig. 10. Annual seasonality factors. Chain line shows proportionate changes in observed incidence and hence the averaged multiplicative seasonality effect. Solid line shows β/β_0, proportional variation in β instantaneously consistent with that seasonal incidence pattern.

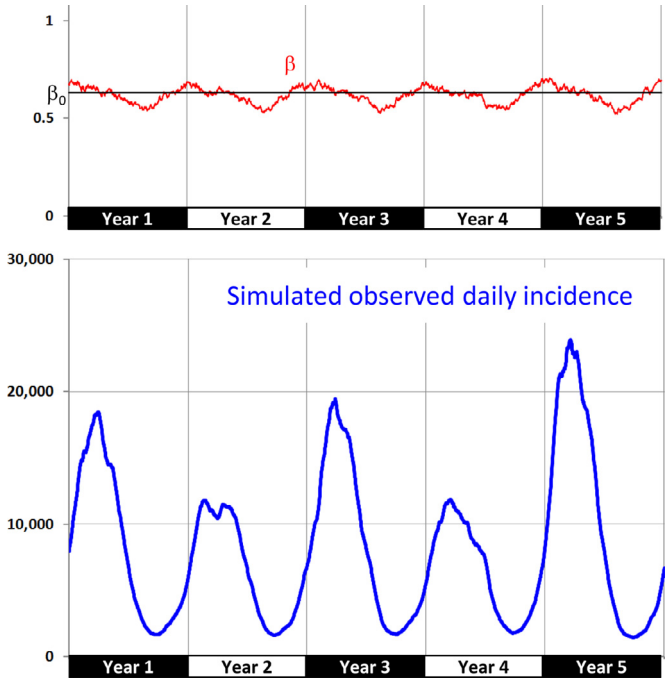

Fig. 11. Reproducing observed NV incidence. Top: values of β with seasonality effect and stochastic variation. Bottom: resulting daily rate from the system dynamics simulation model – compare with Fig. 8.

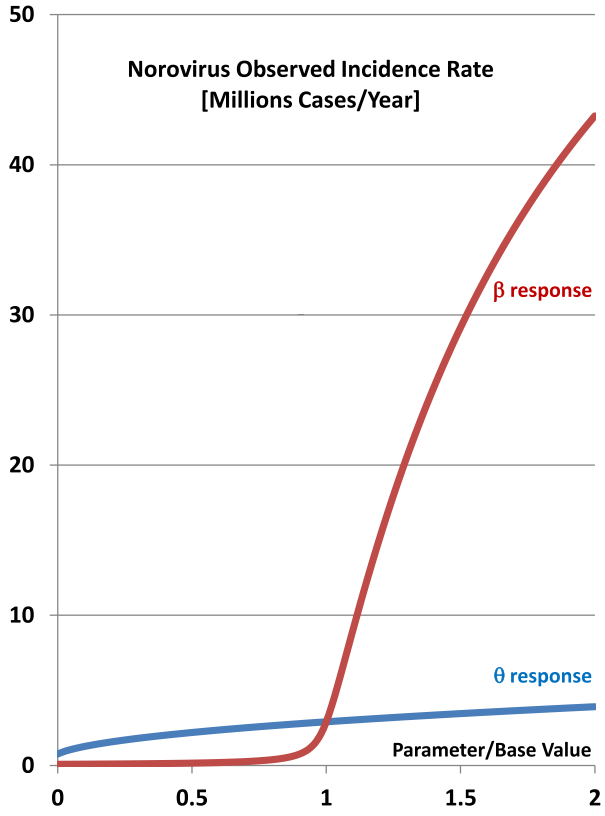

Fig. 12. Observed annual incidence rate against relative sizes of the P2P effect, β and the FB effect, θ.

A similar argument applies to Fig. 7. The right hand side indicates the benefits already achieved by existing advice and infrastructure for the public and/or consumers. Having β fall below β_0 indicates the scale of benefits that might be achieved from improving things further. Clearly P2P transmission merits attention.

Focus now on the shared Base Case point (1, 2.9) and the marginal gains. In Fig. 7, reducing FB effects by 10% reduces total incidence by 4%; a 20% reduction causes a drop of 9%. A 9% reduction in nearly 3 million cases is a significant fall in morbidity and lost work, a gain worth having. Moreover, reducing the foodborne effect by 1/5 is a plausible goal. However, that same marginal calculation can be done using β (Fig. 7). Reducing P2P effects by 10% reduces incidence by 75%; a 20% reduction reduces incidence by almost 90%.

Clearly θ and β have very different sensitivities. This becomes vividly apparent if we use the same scale for the two sensitivities (Fig. 12). Quite clearly, there is much more to be gained from driving down P2P effects, from seeking to move down the β curve. The changes bite more quickly.

Of course, sensitivity to parameter values is not the same as sensitivity to money spent on different types of initiatives, nor does it capture the effort needed to bring about changes. But even though this figure cannot tell the whole story, it still makes a challenging point to the FSA. Using modelling and quantitative analysis it shows the scope of the FB effects with respect to the P2P effects.

Whilst the FB vectors were, naturally, the main interest of the FSA and the focus of the study, this figure poses a significant question for the FSA regarding the effectiveness of trying to control NV infection attributable to food: might it be better to shift the policy focus to P2P effects?

5. Consequences and conclusions

5.1. Recommendations

The modelling and analysis generated recommendations to the FSA, recommendations for how the work could be used and extended.

First, since the model described in Section 3.3 captures current knowledge regarding the causal mechanisms of FB transmission, and represents these in an explicit and comprehensible manner, it should be made generally available.

Second, the scoping work of Section 4 supports the idea that NV incidence can be influenced via FB effects and the modelling work of Section 3 organises the relevant parameters. In support of its 'Foodborne Disease Strategy', the potential policy parameters (Table 1) are where the FSA could target its risk reduction efforts: analysis on the practicality and cost of intervening to change these parameters is appropriate.

Third, the bottom row on Table 1 contains parameter values not currently known. To contribute to agenda-setting and discussions on future research priorities, the table and its underlying modelling should be distributed widely.

The work focused on FB processes. Yet, the scoping analysis of Section 4 (the unexpected contribution to this work) allowed the relative contributions of the FB and P2P effects to be compared quantitatively for the first time – and indicated that the best intervention point for NV might not be via the FSA's territory. The fourth recommendation is that appropriate agencies should consider P2P-style interventions, analysing the practicality and cost of intervening.

Recommendation five is that further work be done on the robustness of the study's findings from the calibrated P2P model. New effects might be included, e.g., partially immune people exposed again to NV may experience a boost in their level of immunity (Menon, George, & Aladin, 2013). Similarly, the uncertainty of parameter estimates should also be explored.

Finally, more simulation modelling work could be useful: for looking again at the seasonality effect and for exploring the sensitivity of NV prevalence to stochastic changes in FB incidence, θ (including the effect of 'shocks' in its value). It is also possible to create a partial endogenisation of FB transmission, allowing for the effect of the various FB reservoirs – the stocks described in Section 3.3 – to be explored.

5.2. Evaluation and actions

FSA elicited an anonymous peer review of the modelling work and the previous sections provide excerpts from this document. We draw further on this now.

The complex, fully endogenised model described in Section 3 demonstrated that modelling the FB mechanisms is possible – a significant achievement in the eyes of the FSA. Moreover, this large model – rather in the manner described by Hodges (1991) – was put to good use: the workshop participants stated that it was useful for understanding pathways of infection, for filling knowledge gaps, and for framing further research requirements.

Implementation of the relevant study recommendations went forward. For example, an extensive description of the 'FSA NoV Model', including complete stock/flow diagrams, and the detailed tabular categorisation of parameters derived from it were made available on the FSA website. A next stage of modelling is being designed, with further FSA support under discussion. The study provided a conceptual framework for FB transmission of NV, and identified potential control points for interventions, as well as current evidence gaps and areas for research. The FSA currently has underway a large attribution study for NV. Expected to be available later in 2018, as well as updating the proportion of NV due to food, it will also help determine the relative importance of the main food transmission routes in the model described in this paper. From this it will be possible to review the work on causal mechanisms and update the model.

Just as the System Dynamics model of Section 3 is a contribution to the NV literature, the work in Section 4 offers a further contribution: the very first empirically-grounded calibration of a P2P model for NV. Indeed, that that same model would hold true outside the UK, and – subject to parameters being available – could be calibrated in the same way.

The scoping analysis described in Section 4 showed that a compact model can give insight (see Pidd, 1999), e.g., into relative sensitivities (with implications for policy interventions) and into seasonality (suggesting that small changes in human behaviour could alone explain the extreme variations). These finding were confirmed in the FSA's review; "The modelling work … identified important sensitivities, non-linear effects and parameter uncertainties". In this way the scoping analysis also acts as a prioritising framework for discussions on very practical interventions. As the review observed, "appropriate selection of sensitivity analysis tests … identified the scale of foodborne versus person-to-person effects and their ranges of influence". It is natural that the FSA is interested in improved hygiene for food picking and processing, how shellfish should be prepared safely, and hygiene in the food service industry. However, what the modelling says about the location of the best policy levers is striking. It suggests that while there are worthwhile improvements to be made on this 'FB front', we are at a point where the benefits are got not just there but might also come from improving P2P hygiene – for example, by encouraging the installation of hands-free taps in toilets. The modelling indicates that it is not just FB transmission that should be targeted but that benefits can be gained by working with other health bodies and considering the virus in the large, with the benefits of targeting P2P effects being judged on the same basis as the benefits for reducing FB effects.

Recent work is aligned with this view. Although the FSA runs its own Twitter feed with advice on safe eating (twitter.com/foodgov), a new initiative uses a different approach (Poppy, 2017). A joint FSA and NHS Choices project actively searches social media data for words relating to NV symptoms ('sick', 'nausea'). Excluding tweets related to other causes (e.g., pregnancy, excessive alcohol consumption), the resulting data is used to provide an early prediction of when cases are increasing. This is in advance of data on Public Health England laboratory reports (the data used in Figs. 1 and 8), by which time implementing any intervention actions may be too late. If the indication is that NV cases will rise then the FSA contacts NHS Digital with the aim of limiting the disruptive consequences of spikes in cases. A range of infographics is posted on social media, in schools and in GP practices. These all suggest ways of soothing the symptoms of NV (stay hydrated, take Paracetamol) and also preventing its spread by both P2P and FB mechanisms (e.g., hand-washing, staying at home if sick). The project is described by two FSA employees on – notably – an NHS Choices webpage (Millson & Staff, 2016), has received noteworthy media coverage (BBC, 2016a; 2016b; Matheson, 2016) and was used in the Winter of 2017/18 (Ward, 2017). Its introduction shows a clear grasp of the idea that interventions in all areas of transmission are worthwhile if NV is to be reduced.

In this paper we have presented the 'complete arc' of this work with the aim of revealing the thinking behind the modelling and analysis, the OR processes and techniques that were used, the unexpected extension of the original research study aims, the insights and practical consequences that have resulted and the further work that is now being designed. We end by recording that the work was received well and deemed a success, particularly in terms of the four aims given in Section 2.3. The FSA's review stated that "The project has fully addressed the original rationale". It mentioned how the model of our Section 3 "improves the understanding of mechanisms" concerning FB transmission. Concerning Section 4 here, the review reiterated that, "intervention in person-to-person virus transmission and associated public health policies, whilst falling outside the FSA's remit, could be as important as foodborne vectors." That insight for the FSA is a significant product of this study. It is a challenging message to report to an organisation whose remit is food, and it was produced by rigorous and effective OR modelling.

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Supplementary materials

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