The application of System Dynamics Modelling approach to understand the brucellosis transmission system

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Author Details

Haitham Taha (The corresponding Author)
The University of Queensland, School of Public Health, Faculty of Medicine, Herston, Brisbane, QLD, Australia
+61 416 460 128
h.taha@uq.net.edu

Simon Reid
The University of Queensland, School of Public Health, Faculty of Medicine, Herston, Brisbane, QLD, Australia
+61 7 336 55551
simon.reid@uq.edu.au

Carl Smith
The University of Queensland, School of Business, St. Lucia, Brisbane, QLD, Australia
+61 7 336 52480
c.smith2@uq.edu.au

Jo Durham
Queensland University of Technology, School of Public Health, Brisbane, QLD, Australia
+61 7 3138 3390
joanne.durham@qut.edu.au

Danielle Currie
Sax Institute, Sydney, NSW, Australia
Danielle.Currie@saxinstitute.org.au

Abstract

Background: Brucella transmission is a complex multisector system. A better understanding of transmission dynamics helps pinpoint the most effective interventions to reduce human cases. Modelling methodologies have not been applied extensively to brucellosis. This paper applies System Dynamics Modelling to identify the interplay between the different sectors that drive disease transmission and suggest and assess scenarios to control brucellosis.

Methods: The study applied a qualitative in-depth analysis of Brucella transmission system in Jordan. Current published literature, government and policy documents were reviewed supplemented by interviews with stakeholders. Data were analysed manually to establish causal pathways to develop a Stock and Flow (SF) model. The structure was examined and reviewed by key informants. Several scenarios to control *Brucella* transmission were assessed.

Results: The model demonstrated the complex interaction of different sectors that drove transmission. *Brucella* transmission among sheep and between farms and markets are the main drivers of human incidence. Farmers' visits to veterinary clinics are a critical intervention point for control regarding access to vaccination. Vaccination by itself might not be efficient due to the low compliance of farmers. Test and cull sheep is the most efficient control strategy.

Conclusions: The synthesis of the current knowledge through the model enabled better understanding, visualisation and interpretation of the sectors involved in *Brucella* transmission. The model highlighted specific leverage points at which the transmission could be controlled like encouraging visits to the veterinary clinics. There is a strong synergy between sectors, therefore, a greater control might be produced by utilising multi-sectoral relationships embedded in the system. This application of System Dynamics Approach to understand disease transmission systems can be used to complement other methods and detect leverage points for disease control.

Keywords

Brucellosis, System Dynamics, Systems Thinking, Epidemiology, causal loop diagrams, disease transmission, infectious diseases, zoonosis.

Key Messages

1. Brucella transmission as a complex system is researched in a holistic view based on the concept of Systems Thinking and System Dynamics Modelling.
2. Interviews with stakeholder were conducted.
3. Qualitative and quantitative data were synthesized and utilized to develop a system dynamics model.
4. A simulation model was developed based on the system structure described by stakeholders and obtained by reviewing the literature.
5. Policies were proposed and assessed based on their simulation outputs.

Introduction

Brucellosis transmits from infected animals into humans through contact or consumption of *Brucella*-contaminated dairy products (Doganay, Aygen, & Eşel, 2001). The most common clinical symptom is recurrent fever (Seleem, Boyle, & Sriranganathan, 2010). It is prevalent in many regions, however, less prioritised and therefore underreported (Pappas, Papadimitriou, Akritidis, Christou, & Tsianos, 2006; WHO, 2006). It infects more than 500,000 people annually, particularly in the Mediterranean and the Middle East. Brucellosis economic significance is related to fertility reduction and decline in livestock production (Franc, Krecek, Häsler, & Arenas-Gamboa, 2018).

Jordan has a high brucellosis burden in livestock and human (Agriculture, 2011). Livestock is of strategic importance accounting for 55% of the agricultural sector (Agriculture, 2011). People traditionally keep sheep to produce meat and milk. Vaccination (Musallam, Abo-Shehada, Hegazy, Holt, & Guitian, 2016) is the only control in Jordan. Although brucellosis risk factors were identified (Al-Majali & Shorman, 2009), they were not discussed in a holistic context and did not provide a dynamic hypothesis to explain the transmission. Moreover, major interactions between sectors to explain transmission over time were not identified.

Brucella transmission is complex (Boschiroli, Foulongne, & O'Callaghan, 2001) due to the interaction of many factors and sectors linked to the infections, like food safety (Brough, Solomon, Wall, Isaza, & Pasvol, 2011) and infected animals (Li, Li, Liang, Fang, & Cao, 2013; Morgan, 1969). Therefore, a comprehensive approach is needed to acknowledge this complexity (Rwashana, Nakubulwa, Nakakeeto-Kijjambu, & Adam, 2014) to achieve effective control (WHO, 2006).

System Dynamics Modelling (SDM) enable understanding complexities (Rwashana et al., 2014) and is enriched by the stakeholders' participation (Newell, Proust, Dyball, & McManus, 2007) to understand the transmission drivers (Maani & Cavana, 2007). This study aims to gain an in-depth understanding of Brucella transmission by engaging stakeholders to develop a dynamic model to suggest control scenarios and provide insights for health officials.

Methods

Systems Thinking (ST) approach was applied, represented by the System Dynamic Modelling. A qualitative in-depth data analysis was conducted by accessing, synthesizing and reviewing published academic literature and available information. The main qualitative data sources included literature and documents review, governmental reports and interviews with stakeholders.

Interviewed stakeholders were identified through the systematic approach proposed by Elias et al (2001) (Elias, Cavana, & Jackson, 2018) and the WHO (WHO, 2012). Key stakeholders were identified by listing all possible eligible stakeholders prioritized by a local governmental expert. A snowball sampling was used to recruit stakeholders not listed previously. An interview guide was developed and 14 interviews were conducted. Obtained data were used to build, develop and inform the stock and flow model (Error: Reference source not found, 2, 3).

The qualitative data was analyzed as proposed by Halcomb, 2006 (Halcomb & Davidson, 2006), by a progressive listening to all fourteen audio-recorded interviews to identify themes (Halcomb & Davidson, 2006). The researcher's notes were incorporated. Inconsistencies were resolved by further elaborations by the participants (Tessier, 2012). Data saturation was confirmed by comparing provided information with new inputs. The model structure was created using Stella software (Chichakly, 2019).

The model was developed as described and explained by Sterman (J. D. Sterman, 2000) and Maani & Cavana (Maani & Cavana, 2007) and implemented in Stella Architect (Version 1.9.1 iSee Systems) (Chichakly, 2019). The software presents model variables and relationships mathematically as integral and differential equations and offers a user-friendly graphical interface (Chichakly, 2019; J. D. Sterman, 2000). The parameters were estimated based on collected data and reviewed from available academic published research and the interviews. Whenever possible, parameters that represent a local measure in Jordan were used, otherwise, parameters were based on globally acceptable estimates identified from literature (Error: Reference source not found).

Model boundaries were checked (J. Sterman, 2000) to ensure incorporating the relevant and endogenous variables in the scope of the complex problem. The model was tested for dimensional consistency, mass-balance, structural assessment, integration error and extreme error tests. Additionally, the overall fit of the simulated behaviour to the reference behaviour was checked (Error: Reference source not found).

Sensitivity analysis was conducted (Maani & Cavana, 2007) to identify the variables most likely influence the model behaviour. Different scenarios were suggested and were compared on the cumulative number of confirmed cases of human brucellosis, the intensity of human brucellosis, brucellosis prevalence in sheep and cumulative sheep abortions.

Results

A modified age-gender structured compartmental model of the Susceptible-Infected-Recovered (SIR) was developed. The model did not account for the economic and environmental aspects. The model has monthly time-step over 12 years starting from January 2004. The reference-mode is the annual number of human cases and the corresponding incidence rate in Jordan from 2004 to 2016 (M. o. H. Jordan, 2018).

Figure 1: Human Brucellosis incidence (per 100,000 people) in Jordan (2004-2016) according to the Ministry of Health (MoH) (M. o. H. Jordan, 2018) .

The model involved Brucella transmission among sheep through the venereal and suckling pathways, therefore, separate sections for ewe, rams and pregnancy pathways were included. A human population model was developed including dairy production section. Public (medical and veterinary) health sectors and the impact of local sheep markets and transboundary entry was incorporated.

Model Subsystems

The model included eight interconnected subsystems, human, ewe and ram, sheep mating & pregnancy, venereal transmission probability, food safety, public health reporting and animal health. Complete structures of each sector are presented in the Appendix.

Model testing

Model boundaries and parameters are adequate, realistic and meaningful. The model does not construct or destruct flows unintentionally. The structure does not violate any natural laws. The model is not sensitive to the changes made on time-dependent calculations or the integration method which indicates model stability. Simulated extreme values resulted in the expected change on reported human and sheep brucellosis. The simulated behaviour predicts the observed behaviour.

Sensitive variables

Sensitive variables by analysis include “Farmers visits”, “Market restrictions”, “Awareness”, “test and cull infected sheep”**,** “slaughter aborted ewe”, “Vaccination” and “Immunity duration”. The proposed policies were developed by combining sensitivity analysis outputs and experts opinion.

Figure 2: Cumulative human cases percent change across each sensitivity variable.

Proposed scenarios

Each proposed scenario reduced reported human cases as shown in Figure 3.

Figure 3: The simulated number of reported cases of human brucellosis under a range of proposed policy scenarios in Jordan**.**

The “One Health” intervention generated the largest reduction (37%) in cumulative reported human cases. The “Enhanced Immunity” scenario generated the smallest reduction (3%). The remaining scenarios reduced human brucellosis in the following decreasing order: “Test and Cull” (29%)> “Awareness” (15%)>“Farmers’ visits” (14%)> “slaughter of aborted” (9%).

Scenarios aimed to reduce infected-sheep directly, “Test and cull”, “Market trade restrictions” and “slaughter of aborted/suspected” were more effective compared to other scenarios with overall reduction (total change) of 154%, 58% and 48%, respectively. The “Test and cull” scenario was the most effective in reducing sheep prevalence (48% reduction) and intensity of human cases (61% reduction). The combined intervention (“one health”) was the second most effective intervention that reduced brucellosis across all scenario measurements by 135%.

Scenarios dependant on human behaviour “awareness” and “farmers’ visits intervention” had a lower case reduction ability, 20% and 17% respectively. The least effective scenario was targeted sheep vaccination (“standard intervention” and “enhanced immunity”) that reduced brucellosis by 16% and 14%, respectively.

The diamond radar graph Figure 4 shows each policy effect (per cent reduction) across all performance measures. The base-case scenario (outermost exterior line) is the reference used for comparison across all policy measurements. It is the observed number of reported cases of human brucellosis in Jordan and the corresponding predicted cases in sheep. The radar graph presents each policy's impact by moving their performance lines closer to the centre when reduction is larger compared to the reference.

Figure 4: Designed policies radar graph across all measures.

The overall reduction was calculated to rank scenarios by overall reduction ability compared to the base case-scenario across intensity, cumulative cases, cumulative sheep abortions and sheep prevalence. The two most effective policy scenarios are "Test and cull" and "One Health".

Table 1: Ranked scenario by overall reduction impact.

Discussion

This is the first SDM study applied to understand Brucella transmission. This study has demonstrated the value of SDM in providing the necessary understanding of the whole system (Rwashana et al., 2014). This is critical because modelling has provided policy-makers with a deeper understanding of the connections between brucellosis system structure, its behaviour and how it changes over time (Burke et al., 2015). It offered a valuable method to understand transmission and to overcome many ethical and other anticipated limitations (Borshchev A, 2004; J. Sterman, 2000). It is a valuable tool to explore multiple interventions to enable decision-makers to make informed decisions and to visualise the likely future (Borshchev A, 2004). The model overcame data-shortages and uncertainty about brucellosis system by allowing the integration of several forms of evidence, such as expert opinion and governmental reports (Homer & Hirsch, 2006).

Previous epidemiological studies focused on the direct relationship between disease agent, vector and host (Park et al., 2005; Yoo, Heo, Lee, Kim, & Yoo, 2015). Similarly, most brucellosis studies, particularly in Jordan, were designed to identify risks (Kaden et al., 2014; Leong et al., 2015; Shin, Kwag, Park, & Kim, 2017). These studies did not explain embedded complex relationships that drive transmission dynamics, particularly the feedback links between the disease and the characteristics of the sectors involved. This study demonstrated the non-linear relationship between the bacterium, sheep and people and as a continuous complex interaction between Brucella sectors such as food safety (Brough et al., 2011), animal infection (Morgan, 1969), other risk factors (Li et al., 2013) and the health systems (animal and human).

The simulation suggested a cyclic behaviour of incidence every 3-4 years, unlike previous studies that reported brucellosis only annually (M. Jordan, 2018) as a seasonal effect of breeding (Abu Shaqra, 2000). The model accounted for the holistic involvement of the sectors to describe oscillatory behaviour. This is important because conventional theory associates only lambing seasonality to human brucellosis incidence (Abu Shaqra, 2000), while multi-year cyclical behaviour can explain longer-term effects such as vaccination delays and population behaviours (Awareness). This helps to conduct more accurate risk assessment studies that account for such delays theoretically and practically.

Policy Scenario discussion

Scenario one: Farmers visit intervention

The identified triad link between farmers' visits, vaccination and human cases has not been identified as a major factor of disease dynamics previously. This association connects farmers to veterinary services (Svensson, Lind, Reyher, Bard, & Emanuelson, 2019) as focal points for sheep vaccinations. This suggests sheep vaccination rates might indirectly improve by encouraging farmers' visit. Seeking veterinary services however is not typically a priority for most farmers (Kebede, Melaku, & Kebede, 2014), particularly when they suspect brucellosis, due to fear that their animals will be culled without compensation (Beauvais, Musallam, & Guitian, 2016).

Scenario two: Market trade restriction

Unlike other studies in Jordan, local markets involvement in brucellosis was explored. Markets may facilitate local and international sheep movement and mixing (Franc et al., 2018). Therefore, banning the trading of infected sheep could significantly lower consumption and contact risks. This dual effect led to greater simulated reductions in sheep abortions, brucellosis prevalence (sheep) and the incidence of human cases (16%, 19% and 11%, respectively). Trade surveillance and restrictions are valuable strategies to control brucellosis (Health, 2020). Recent studies associated high infection rates to widespread uncontrolled informal sheep trade (Musallam, Abo-Shehada, & Guitian, 2015). The simulated "market restriction" scenario successfully reduced brucellosis by 58% and is ranked the 3rd best scenario. These results highlight the importance of controlled trade, therefore, greater attention should be directed to limit risks of the established irregular sheep markets by restricting irregular trades locally and across borders, as currently there are no restrictions on formal or irregular sheep trade in Jordan.

Scenario three: Awareness of farmers' intervention

Awareness and knowledge have been shown to reduce infection risks and improve health (Lu et al., 2009; Zhang, Zhou, Huang, & Guan, 2019). However, previous studies found that only 38% of the farmers in Jordan are aware of brucellosis, mainly through advertisements, doctors' and veterinarians' advice (Musallam, Abo-Shehada, & Guitian, 2015). Improved awareness in the model simulation reduced only human cases because it improves personal hygiene and personal protective equipment use only. These results are supported by the WHO recommendations to improve public health education and awareness programs to reduce the risk of exposure and consumption to control brucellosis (WHO, 2006).

Scenario four: Test and Cull intervention

The results of the "test and cull" intervention showed the greatest overall reduction in brucellosis in both human and animals (61% and 48%, respectively). This intervention reduces disease intensity because it was designed to cull infected ewes, which directly reduced brucellosis prevalence and eliminated consumption and contact risks. These results are plausible given that culling infected sheep to eliminate brucellosis is considered a highly effective control strategy (Dieste-Pérez, Frankena, Blasco, Muñoz, & de Jong, 2016; Manual, 2020). In Jordan, there are no national campaigns or strategies to cull infected animals (Beauvais et al., 2016). However, most sheep owners voluntarily cull diseases (aborting) sheep by at-home-slaughter or they sell it to a butcher (Musallam, Abo-Shehada, & Guitian, 2015). The absence of suitable compensation programs for farmers is one of main implementation and enforcement challenges of such programs, as many farmers will not approve culling of their sheep without compensation, particularly if the illness is not apparent (Johansen & Penrith, 2009; Musallam, Abo-Shehada, & Guitian, 2015). Moreover, forced culling without compensation may lead to increased illegal animal movements that would increase the rate of disease transmission (Penrith & Thomson, 2004). Therefore, although culling is the most cost-effective strategy to control brucellosis, several economic, social and other factors should be evaluated before selecting this strategy for implementation (Manual, 2020). This study provides reasonable justification that this program could be considered as an option to control brucellosis in Jordan, however, there is a need to consider financial compensation.

Scenario five: Slaughter of aborted/suspected sheep

Previous studies have shown that most farmers in Jordan prefer managing brucellosis independently rather than calling a veterinarian (Bard et al., 2019). This is because of a lack of trust (Svensson et al., 2019) associated with the fear of slaughter of infected sheep without compensation, and the perception that the brucellosis vaccine causes abortions (Musallam, Abo-Shehada, & Guitian, 2015). The simulation showed that non-supervised in-house sheep slaughter less effective compared to other scenarios because it is completely run by farmers without professional supervision, and farmers often do not evaluate risks posed by keeping infected sheep properly compared to the financial losses perceived by slaughtered sheep (Svensson et al., 2019).

Scenario six & seven: Vaccination and immunity effectiveness

Sheep vaccination is the main control strategy in Jordan (Beauvais et al., 2016). Although successful, previous studies showed a very low coverage (< 2%) and low efficiency of vaccination programs (Musallam, Abo-Shehada, Omar, & Guitian, 2015). Likewise, simulation of the vaccination and immunity scenarios are unlikely to be effective even by extending immunity duration of the vaccine (the new strategy adopted in Jordan). This is attributed to the vaccinations conducted only at veterinary clinics since regular national vaccination campaign are very limited (Beauvais et al., 2016). Therefore, vaccination is the farmers' responsibility and dependant on their compliance and commitment. This creates problems with implementation and vaccination even though vaccines are provided free of charge (Agriculture, 2011). Farmers' compliance is a fundamental requirement of a successful control strategy including vaccination. Therefore, unless there is good compliance of farmers, sheep vaccination and immunity strategies may remain inefficient.

Scenario eight: One Health

Most of the organisation like the WHO has a continuous and increasing interest of health programs that apply the "One Health" approach ("WHO | One Health," 2017). One of the most significant findings of this study is the inclusion of a “One Health” control strategy. The “One Health” scenario reduced human brucellosis significantly and is the second most effective scenario across all policy measures (135% reduction). It included interventions from several sectors of the system that had a synergistic effect. These results are consistent with previous studies that recommend “One Health” management approach to prevent epidemics and epizootics (Destoumieux-Garzón et al., 2018). Other studies concluded that the application of holistic and multiple-scale approaches like “one health” enabled the control of several infectious diseases such as schistosomiasis and avian influenza (Destoumieux-Garzón et al., 2018; Ryu, Kim, Lim, Tan, & Chun, 2017). This “one health” intervention involved the main pillars of the “One Health” approach, human (awareness), animal (slaughter and immunity) and the environment (markets) (Ryu et al., 2017). These results emphasize the significance of “One Health” approach and the importance of the multi-sectoral relationships embedded in the system that drives its behaviours and propose to achieve better outcomes in both, human and animal sectors. Therefore, stakeholders should be directed toward a new paradigm that shifts their mental models from considering one-sector responsibility (MoA) to become the responsibility of all involved sectors.

Recently in Jordan, efforts were guided towards the “One Health” approach to map-out current networks and explore points of communication, coordination and decision-making that permits several sectors and stakeholders to act interactively, and investigate priorities and gaps which limits sharing information (Sorrell et al., 2015). Despite the existence of the informal communication across sectors, particularly at emergencies, formal routine coordination was absent. Therefore, these findings set foundations and directions for coordination and potentials benefits and outcomes of adopting the "One Health" approach. Additionally, these results provide theoretical evidence of the usefulness of the "One Health" approach in public health interventions.

Conclusions

This is the first SDM study applied to understand brucellosis. This research identified unexplored interventions to control brucellosis by understanding the system dynamics. The main aim of SDM is to help people understand and to create change in mental models. This model was designed to be a tool to support decision-makers to understand the underlying feedback mechanisms in the brucellosis system and to serve as a tool for policy design to enables scenario analysis and assessment.

The observation - that the current government policy of managing brucellosis through vaccination of sheep will be ineffective - is important because it means the strategy is unlikely to achieve the expected prevention levels. The simulation suggests that the strategy relying on the dynamics between farmers and veterinary clinics to deliver vaccination will fail therefore a proactive national vaccination campaign is required.

The effectiveness of testing and culling infected sheep to control brucellosis confirms the strategy recommended by international organisations such as the OIE and WHO. However, the implementation should only be considered after a thorough assessment of the economic impacts to ensure adequate compensation is available to farmers. It would also demand well-organised multisector cooperation and high cost, therefore, difficult implementation in Jordan. However, the test and cull strategy could be considered as part of a future direction for the government if brucellosis becomes a higher priority for public health. The demonstration of the strong synergy between sectors involved in brucellosis highlights the need for the "One Health" approach that leads to the articulation of shared interest with a common goal to reduce brucellosis burden in Jordan.

Conflict of Interest

No conflict of interests

Ethical clearance

Ethical approval to conduct this research was obtained from the National Health and Medical Research Council in Australia (NHMRC) (Approval Number: 2018000990).

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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