IDENTIFYING RISK INTERDEPENDENCIES IN PHARMACEUTICAL SUPPLY CHAINS THROUGH GAMIFICATION-ENABLED STRUCTURAL MODELLING

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ABSTRACT

We develop an approach for the evaluation of interrelated risks that could compromise a pharmaceutical supply chain’s ability to serve patients, whereby experts conduct pairwise-comparisons through an online gamification-enabled platform. Risks categorization based on structural modelling elevates their consideration beyond the single instance in which they are normally evaluated.

KEYWORDS: Multi-method research, Pharmaceutical Supply Chains, Supply Risk Management

INTRODUCTION

The literature on risk management in supply chains has developed substantially in recent years demonstrating the importance of taking a systems perspective on risk. For example, since the seminal work of Craighead, Blackhurst, Rungtusanatham, & Handfield (2007) increasing attention has been paid to the network characteristics of supply chains, and how these characteristics may affect system-wide disruptions. In a similar fashion, the World Economic Forum (2018) highlights that global risk perception should take into account how different risks might influence each other, as if forming a network, rather than evaluating each risk in isolation in terms of frequency and magnitude. Interdependencies between individual risks are sometimes acknowledged (for example, Chopra & Sodhi 2004), but not generally considered. The pharmaceutical sector provides an ideal context to address this methodological gap. Pharmaceutical Supply Chains (PSC) are increasingly exposed to disturbances such as the contamination, adulteration and substitution of pharmaceutical ingredients throughout increasingly global sourcing processes; the intentional and fraudulent production of drugs (counterfeiting); and the manifestation of arbitrage behavior through speculative inventory build-up in secondary distribution channels (Marucheck, Greis, Mena, & Cai, 2011). Due to the fragmented nature of PSCs, it is not common practice to analyze the identified risks in terms of possible interdependencies between them. Rather, the industry’s approach to risk management is predominantly concerned with Good Manufacturing Practice (GMP) and regulatory compliance (Friedli, Basu, Belm, & Werani, 2013, p. 63). Whilst relationships between risks are sometimes defined in hierarchical terms as in Fault Tree Analysis (Rees, 2011, p. 403), these approaches lack consistent analytical counterparts.
Considering the above mentioned gaps, we develop an approach for identifying and evaluating risk interdependencies that could compromise a PSC’s ability to serve patients. This is achieved by answering the following research questions:

- **RQ1:** How can PSC risks be categorized and prioritized while systematically taking into account the interdependencies between them?
- **RQ2:** Which areas of interventions become more prominent when risk interdependencies are taken into account?

The proposed approach is meant to inform the formulation of mitigation strategies by elevating the consideration of risks beyond the single instance in which they are normally assessed. The reminder of this paper provides an overview of the relevant academic literature; outlines key methodological aspects for the elicitation and analysis of expert knowledge on risk interdependences; and illustrates an initial implementation through a sector case study in the UK pharmaceutical industry. This is followed by a discussion of some preliminary findings, and the expert feedback on how such findings may inform a critical appraisal of current and perspective risk mitigation practices.

**LITERATURE REVIEW**

Compared to the vast academic literature on Risk Management in Supply Chains (Heckmann, Comes, & Nickel, 2015 provide an overview), relatively little work has investigated the nature and prevalence of risk in pharmaceutical supply. For example, Huq, Pawar, & Rogers (2016) surveyed senior PSC executives on 20 ‘disturbance factors’ in three global pharmaceutical network configurations differing for outsourcing location policy; Panzitta et al. (2017) propose a simplified risk assessment procedure to help regulators to quickly assessing medicine shortage risk in relation to 10 factors potentially affecting manufacturing complexity; Breen (2008) mapped out the PSC underpinning the UK National Health Service and identified 35 aspects of the current ‘state-of-the-world’ that could negatively affect the movement of medicines and materials, and hence compromise the treatment of patients. Jaberidoost, Nikfar, Abdollahiasl, & Dinarvand (2013) identify 50 vulnerability areas of a PSC by reviewing the literature. While a comprehensive overview of the literature is left outside the scope of this paper for brevity, it is possible to outline broad trends from both a conceptual and a data-driven modelling perspective:

- From a conceptual perspective, a common trait across research carried out to date, regardless of specific applications to PSC, is that the emphasis is placed on identifying and categorizing disturbances, chiefly uncertain and adverse triggering-events and outcomes, which are aggregately addressed with the blanket term ‘supply chain risks’.
- From a modeling perspective, there seems to be three incumbent perspectives on data-driven supply chain risk management in PSC, namely:
  - **Statistical inference and predictive analytics:** empirical observations such as time-series or longitudinal data are mined to detect regularities in the occurrence of specific events. With regards to the pharmaceutical industry, regulatory agencies provide public domain datasets regarding, for example, medicine shortages and recalls. The analysis of such data with the aim of identifying trends and developing predictive analytics has received little attention in academia (Aschenbrücker, Löschner, & Troppens, 2013);
  - **Simulation and optimization:** probabilistic and ‘snapshot’ data (i.e. not historical) concerning the occurrence of identified scenarios are commonly taken into account when optimizing supply network configuration or simulating inventory dynamics in the form of stochastic programming and chance constraint. Applications may include avoiding medicines shortage by optimizing the build-up of buffer inventory as a mitigation strategy. For example Bam, McLaren, Coetzee, & Von Leipzig (2017) apply Systems Dynamics to model shortage risk for tuberculosis medicines;
Expert judgment: In the absence of precise quantitative data about specific product supply chains, the two approaches mentioned above cannot be applied. Often, the only source of empirical evidence is the expertise of those ‘in the know’, which then needs to be appropriately elicited and processed to provide some aid to decision making. Expert judgment may be elicited in the form of qualitative data, as in interviews or panel studies (Breen, 2008); or semi-quantitative data such as scores on ordinal scales as in surveys (Huq et al., 2016) and pair-wise comparisons (Raka & Liangrokapart, 2017). The last perspective is of particular relevance for this paper, since empirical evidence is gathered chiefly through expert judgment. The reason for this choice is twofold. First, the necessary data for simulation and optimization is often company and product-specific: while providing greater accuracy, this approach may limit a priori the possibility to gather a broader, multi-stakeholder perspective on the topic of risk in PSC. Second, most statistical datasets available in the public domain have geographical coverage limited to the United States, and lack an end-to-end supply chain perspective. Rather, these datasets focus on the occurrence and duration of specific events such as shortage and recall of pharmaceutical products, sometimes accompanied by the indication of a single cause for its occurrence (for example, ‘manufacturing delay’, ‘demand variability’ etc.).

MATERIALS AND METHODS
The multimethod research approach adopted in this paper for modeling PSC risk is illustrated schematically in Figure 1.

Figure 1: Visual summary of proposed approach

The following sub-sections illustrate the key methodological aspects of the proposed multi-method research approach with regards to terminology and conceptual assumptions; techniques for semi-quantitative analysis; and data gathering process.

Theoretical perspective
In the context of this research, the notion of PSC risk is chiefly associated with the ability or inability to provide patients with the ‘right’ medicines. While risk is relatively straightforward to formulate mathematically, it is more difficult to reach agreement on contextual definitions that enable the effective management of risk in supply chains (Kumar, Srai, & Gregory, 2016). A widespread attitude towards the concept of risk is to place the emphasis almost exclusively on what can go wrong, and hence on what supply chain organizations need to worry about (Olson & Wu, 2010). Underneath this common understanding of risk is the belief that unacceptable outcomes must have unacceptable causes, and that these
must be distinct from the causes of acceptable outcomes, thus reflecting an implicit moral codex in which good deeds are rewarded and bad deeds are punished (Hollnagel, 2018). This belief is implicitly endorsed in PSC through commonly adopted managerial practices such as root cause analysis – see for example Friedli et al. (2013). The main methodological implication of this terminological habit is that hunting for broken components within complex socio-technical systems continues to equate with ‘good analysis’ (Dekker, 2011).

A more nuanced view is that undesired outcomes typically associated with the notion of ‘risk’ emerge from the behavior of a complex socio-technical system, hence making ‘things that go wrong’ hardly separable from ‘things that go well’ (Hollnagel, 2018). Fewer works have brought to the fore the role of structural elements reflecting the system-like nature of supply chains in general, and PSC in particular. For example, Craighead, Blackhurst, Rungtusanatham, & Handfield (2007) associate the occurrence of supply chain disruptions, as well as the ability to respond to such disruptions through mitigation capabilities with structural elements of supply chains across several industries, including pharmaceutical, such as density, complexity, and node criticality.

The terminological caveats examined above lead to the following conceptual assumptions, which are adopted henceforth:

1. The term ‘risk’ more appropriately describes the exposure to the chance of loss or gain by choice rather than fate: in this way the attention is shifted towards managerial aspects for which decision support tools are needed (Emblemsvåg, 2011);
2. Supply chains being complex socio-technical systems (Pathak, Day, Nair, Sawaya, & Kristal, 2007), focusing on linear cause-effect relationships to understand adverse and disruptive outcomes can be misleading. Rather, it is necessary to pay greater attention to both the relevant system’s elements, and the contextual relations among them;
3. Higher-order interactions between ill-defined elements of a complex system are difficult to grasp relying on the individual’s bounded rationality. To explore these interactions, experts need to sharpen their perception of the relationships between the system’s elements through a formalized structure (Bolaños, Fontela, Nenclares, & Pastor, 2005).

Techniques for semi-quantitative analysis
The theoretical perspective presented above is addressed here through Structural Modeling (SM). A common principle across various SM techniques is to enable a group of experts to formally articulate an ill-defined problem in terms of elements and relationships within a system using the principles of graph theory, while allowing each expert to contribute diverse data, skill, and knowledge – see Lendaris (1980) for a comparative overview.

Specifically, two closely related techniques will be considered here:

- the structural problematique analysis developed within the DEMATEL (Decision Making Trial and Evaluation Laboratory) project (Fontela & Gabus, 1974), and
- the MICMAC (Matrice d’Impacts Croisés-Multiplication Appliquée à un Classement) technique (Godet, 1977).

Both approaches take inexact, subjective inputs with the aim of producing a meaningful, but not precise output by ranking, categorizing, and visualizing the elements included in the system of interest based on how they relate to each other. In both cases, the system’s elements are typically qualitative structural variables of memory and experience, anticipation and foresight, or needs and goals; the relationships between such elements are typically relational statements can be definitive, comparative, influential, or mathematical in nature.

The key difference between MICMAC and DEMATEL is in the classification/prioritization and visualization of the elements of the system based on their interrelationships. In particular:

- **Visualization facilities:** both MICMAC and DEMATEL generate classification planes with specific interpretations for different areas of the plane;
• Computational structure: DEMATEL is based on solving a convergent series the elements of which are powers of a normalized cross-impact matrix. Conversely, MICMAC is based on raising a cross-impact matrix to consecutive powers following specific stopping criteria;
• Procedural consistency: DEMATEL is probably the approach more accurately described since the outset from a computational perspective. The consistent application of MICMAC is difficult to verify, as most works in the literature do not disclose the analytical details of the steps followed (see for example Jain, Kumar, Soni, & Chandra, 2017).
• Synthesis of multiple responses: DEMATEL explicitly provides analytical devices to combine multiple responses obtained from different experts, and to deal with the uncertainty deriving from such variety. In principle, also MIMAC and ISM may involve multiple experts, but it is unclear how this is analytically taken into account.

Based on our literature review, neither DEMATEL nor MICMAC have been applied to evaluate risk interdependencies in PSC. While System Dynamics qualifies as an SM tool (Lendaris, 1980), its applications to PSC are either product-specific (Bam et al., 2017), or purely schematic representations of causal paths and feedback loops (Narayana, Arun, & Rupesh, 2014).

Data gathering process
The identification of relevant risks with specific regards to the PSC was carried out through an iterative process involving multi-stakeholder workshops; qualitative data analyses through text mining; and online collection of semi-quantitative data (ordered-category rating items) through gamification-enabled structural modelling. Workshops were deemed a suitable format to gather reliable data through the active participation of a selected group of individuals sharing common expertise in the domain of interest (Ørngreen & Levinsen, 2017).

The steps of the knowledge elicitation process can be summarized as follows:
• Identification of risk elements to generate a ‘risk universe’ for a generalized PSC using a standardized PSC configuration map (Srai & Gregory, 2008) within a semi-structured workshop process involving input from multiple experts with extensive experience on risk analysis across the sector. Experts included individuals from two of the largest UK-based medicine manufacturers; a leading specialist healthcare distribution logistics providers; the major pharmacy retailer in the UK; a healthcare consultancy practice providing analytical tools for risk management; and a financial institution specializing in pharmaceutical risk insurance and reinsurance.
• Over 120 hours of expert deliberations on risk events informed the development of a ‘universe’ or risks, generating 121 risk items (statements) across the end-to-end PSC. In line with the incumbent risk management practice and academic literature alike, the risk universe thus obtained represented a comprehensive list of ‘things that can go wrong’ in a PSC, each accompanied by a definition and supporting statement of possible root causes. The potential relationships between these items were not identified at this stage;
• Textual data analysis: standard text mining techniques (Provost & Fawcett, 2013 Ch.10) were deployed to evaluate wording similarity and discover possible latent topics across items included in the workshop’s risk universe, as well as in relation to 13 similar lists published in the academic literature. Through multiple iterations informed by the text mining results, 74 risk items aggregated in 17 categories were selected as elements of the system of interest to be further analyzed through SM. The items and categories included in this subset of the risk universe are listed in the Appendix;
• Pair-wise comparison of selected risk item: a second data-gathering process involved a group of five experts representing primary and secondary manufacturing; distribution and retail pharmacy, and institutional sector risk consultancy. The experts were required to provide \( N = n(n - 1) \) scores on a scale from 0 [no influence] to 5 [very strong influence], where \( n = 74 \) is the number of risks included in the final list. A gamification-enabled online
platform for structural modelling (MATRisk: https://remedies-ifm.azurewebsites.net/) was specifically developed to enable the assessment of the level of interdependence between risks by pair-wise comparison. Elements of gamification were specifically introduced to incentivize users to engage in the process of collecting data of greater quantity and quality (Seaborn & Fels, 2015). In particular, through the online platform, each respondent scored remotely and in their own time the N pairs of risk items. Each pair was presented on screen as a ‘card’ containing an iconic representation and textual description of each item. The pairwise comparisons between these items was operated either by simply ‘swiping left’ to indicate that no association between the items exists, or ‘swiping right’ otherwise – in which case the respondent is asked to score the magnitude of the association on a 5-point ordinal scale. To expedite the process, experts could swipe groups of items simultaneously by using top-level cards corresponding to the 17 categories previously identified. The second process step in Figure 1 provides an iconic representation of the proposed gamification-enabled pair-wise comparison.

The preliminary data gathered process was carried out over 20 days throughout April 2018, following a webinar organized by the researchers to illustrate the purpose and use of the online platform to the enrolled respondents. At the end of the time window, data was gathered in the form of cross-impact matrices, analyzed by the researchers and the results presented to the respondents for feedback in a follow-up validation workshop.

RELIMINARY FINDINGS

To address RQ1 and RQ2, this section provides insights into the process of generating a classification and prioritization of PSC risks from experts-generated interdependencies scores. For the sake of clarity, the analysis is illustrated through a streamlined example first, and later on applied to actual data obtained from one respondent through the MATRisk online platform. For illustration, assume the risk universe consist of 7 items; then a hypothetical expert response corresponds to a 7 × 7 cross-impact matrix \( X \) like the one depicted in Table 1. (An actual table gathered through MATRisk would have 74 × 74 = 5,476 cells: due to space limitations, such table is not reported in full here, but is available from the authors on request)

<table>
<thead>
<tr>
<th>EXP</th>
<th>Influencing risk item</th>
<th>Influenced risk item</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td>Critical findings during Quality Audit</td>
<td>0</td>
</tr>
<tr>
<td>D</td>
<td>Process variability and quality deviation</td>
<td>0</td>
</tr>
<tr>
<td>A</td>
<td>Final product contamination/degradation</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>Supplier’s understanding of regulatory constraints</td>
<td>3</td>
</tr>
<tr>
<td>C</td>
<td>Strategic/commercial decision by supplier to discontinue product</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>Lack of process robustness/process failure/variability of product</td>
<td>0</td>
</tr>
<tr>
<td>E</td>
<td>Shelf life insufficient for product lifetime/distribution timescales</td>
<td>5</td>
</tr>
</tbody>
</table>

EXP: expert classification by cause/responsibility (A - Failure in Focal Company Quality; B - Failure in Contract Manufacturer quality; C - Inability of supply; D - Process complexity/variability; E - Regulatory Change).

Table 1 shows an example of how most SM techniques, such as DEMATEL and MICMAC, formally articulate the relationships of direct influence between any pair of constituting parts of the problem situation. Each cell in the cross-impact matrix records the expert’s assessment of the influence of the item listed row-wise on the item listed column-wise. Hence, the generic element of a cross-impact matrix \( X \) can be interpreted as follows:
In equation (1), each row and column of \( X \) (hence, each risk item) is indexed as \( i \) and \( j \), respectively. The estimate \( l \) of the magnitude of a relationship between elements of a problem situation is typically expressed using ordered-category rating items. Unfortunately, there is no consistent use of rating items in the literature. Depending on the individual study, the rating items range from \([0, 1]\), indicating just the absence/presence of an influential relationship (see for example Jain et al., 2017), and up to 5-points ordered-category rating items to indicate very low \([1]\) to very high \([5]\) influence (see for example Rajesh & Ravi, 2017). The latter type of rating item is not be confused with Likert-type scales used in survey research, since it lacks the characteristic of being a bipolar and symmetrically balanced response set, and it is not meant to indicate degree of agreement with a stimulus attitude statement.

For example, \( x_{25} = 2 \) denotes that, in the expert’s opinion there is a direct influence between risk item 002 (‘Process variability and quality deviations’) and risk item 005 (‘Strategic/commercial decision by supplier to discontinue product’). While this is not the case the other way round, since \( x_{52} = 0 \). Mutual influences are allowed, but the relationship is not symmetrical i.e., ‘A influences B’ does not imply that ‘B influences A’. In terms of the MATRisk online platform usage, this means that the respondent has ‘swiped right’ when presented with a the pairwise comparison card stating ‘Risk item 002 influences risk item 005’, but they ‘swiped left’ when presented with the card stating the relationship the other way round. Consequently, along any row of matrix \( X \) one reads the direct influence exerted by the corresponding risk item on any other item; along any column, one reads the dependence of the corresponding risk item on any other item. In the example, item 002 directly influences items 005 and 006 (‘Lack of process robustness/process failure/variability of product’); and it directly depends on items 005, hence 002 and 005 are said to form a cycle. Matrix \( X \) can, in fact, be interpreted as the incidence matrix of a weighted directed graph. For an actual response, Figure 2 shows the network visualization and descriptive analysis generated using Gephi (Bastian, Heymann, & Jacomy, 2009).

The use of graph-theory to interpret the cross-impact matrix \( X \) is a key principle of SM in general (Lendaris, 1980), and of techniques such as MICMAC and DEMATEL in particular. Both techniques take \( X \) as input, but then process it in a slightly different fashion: According to the MIMAC technique, \( X \) is raised to successive powers \( p = 2, 3, \ldots \) to unravel paths of influence beyond the direct connections represented in the corresponding graph. For example, making reference to the hypothetical example in Table 1, risk item 002 does not exert a direct influence on item 003 (‘Final product contamination/degradation’) but it does so indirectly through item 006, which it directly influences and, in turn, influences item 003. This is known as transitivity. This path can be discovered through the Boolean operation of raising \( X \) to the power \( p = 2 \), and checking that \( x_{23}^{(2)} \neq 0 \) – here the notation \( x_{ij}^{(2)} \) denotes the element in row \( i \) and column \( j \) in the Boolean matrix associated with \( X^2 \), not \( (x_{ij})^2 \). This leads to the following general formulation:

\[
T^{*} = \lambda X^{p^{*}}
\]  

(2)

Where \( T^{*} \) is the normalized matrix of total connections, \( p^{*} \) is the highest power to which matrix \( X \) is raised; and \( \lambda \) is a normalization factor. Unfortunately, there is no agreement in the literature with regards to the parameters \( \lambda \) and \( p^{*} \).
For example, Godet (2007) suggests that $p^*$ is such that greater powers no longer affect the ranking of the vector sums across the columns and rows of $\mathbf{T}^*$, whereas Lendaris (1980) implies that $p^* = n$; in either case $\lambda = 1$. Conversely, (Hachicha & Elmsalmi, 2014) use $\lambda = 10^{-p^*+1}$ but do not provide a general rule. Other applications do not disclose the computational procedure followed in implementing MICMAC. In the simplified example considered here, $p^* = 4$ is found iteratively. It follows that $\lambda = 10^{-3}$ and:

\[
\mathbf{T}^* = \begin{bmatrix}
0.625 & 0 & 0.025 & 0 & 0 & 0 & 0.250 \\
0.500 & 0.225 & 0.300 & 0 & 0 & 0 & 0 \\
0.625 & 0 & 0 & 0 & 0 & 0 & 0.125 \\
0.075 & 0 & 0.075 & 0 & 0 & 0 & 0.375 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0.125 & 0 & 0.090 & 0.225 & 0.800 \\
0.125 & 0 & 0.125 & 0 & 0 & 0 & 0.625
\end{bmatrix},
\]

\[
\mathbf{d}^* = \begin{bmatrix} 1.95 \\ 0.22 \\ 0.62 \\ 0.09 \\ 0.09 \\ 0.22 \\ 2.17 \end{bmatrix},\quad \mathbf{r}^* = \begin{bmatrix} 0.90 \\ 1.02 \\ 0.75 \\ 0.52 \\ 0 \\ 1.21 \\ 0.87 \end{bmatrix}.
\]

Vectors $\mathbf{d}^*$ and $\mathbf{r}^*$ are obtained, respectively, as the column and row sums of $\mathbf{T}^*$, providing for each item in Table 1 a measure of its overall power of influencing or being influenced, directly and indirectly, by any other items. The elements in $\mathbf{d}^*$ and $\mathbf{r}^*$ that correspond to a specific risk item are used as coordinates to graphically represent the item on a Cartesian plane. For an actual respondent, Figure 3 (next page) shows the risk items scatterplot on the influence/dependence plane.

In Figure 3 the risk items are categorized as they fall into specific quadrants of the plane based on whether their coordinates are above or below the average dependence and influence. Proceeding clockwise, each quadrant is interpreted as follows (Godet, 2007):
Figure 3 MICMAC risk categorization for initial response (risks list in Appendix)

- Quadrant I (upper-left): mostly *influential* items, potentially conditioning and explaining the behavior of the whole system;
- Quadrant II (upper right): gate-keeping or *relay* items showing instability, characterized by being both influential and dependent on other items in the system;
- Quadrant III (lower right): mostly *dependent* items, largely resulting from the interactions between those items in quadrants I and II;
- Quadrant IV (lower left): mostly *autonomous* items, that may be expected to have little or no influence on future developments having fewer relationships with the rest of the system.

These can be safely discarded from further analysis.

The segments corresponding to each quadrant are visually codified as shapes in Figure 3. The same matrix-structured dataset gathered through the MATRisk app was analyzed through the DEMATEL technique. A distinguishing feature of DEMATEL is that the total connections matrix $T^*$ is the result of a convergent series, the element of which are powers of a normalized cross-impact matrix $A$ obtained by multiplying the raw data gathered in $X$ by a scalar equal to the reciprocal of the largest row sum of the cross-impact matrix (Fontela & Gabus, 1974):

$$T^* = \lim_{p \to \infty} \left( A + A^2 + A^3 + \cdots + A^p \right) = A(I - A)^{-1} \quad (3)$$
In equation (3), \( \mathbf{I} \) is an identity matrix of adequate size, and the superscript \(^{-1}\) denotes matrix inversion. The aspects of normalization and convergence criteria when computing the total connection matrix as shown in equation (3) are less ambiguous in the literature than in the MICMAC case. As in the MICMAC case, the key metrics of dependence and influence are obtained by summing the elements of the total row and column-wise, respectively. Using the simplified example in Table 1, from equation (3) one obtains:

\[
\mathbf{T}^* = \begin{bmatrix}
1.39 & 0 & 0.34 & 0 & 0 & 0 & 1.95 \\
0.71 & 0.44 & 0.69 & 0 & 0.41 & 1.20 & 1.01 \\
1.22 & 0 & 0.17 & 0 & 0 & 0 & 1.71 \\
1.02 & 0 & 0.14 & 0 & 0 & 0 & 0.83 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
1.01 & 0.61 & 0.96 & 0 & 0.17 & 0.44 & 1.41 \\
1.71 & 0 & 0.24 & 0 & 0 & 0 & 1.39 \\
\end{bmatrix}; \quad \mathbf{d}^* = \mathbf{1}^\prime \mathbf{T}^* = \begin{bmatrix} 7.09 \\ 1.06 \\ 2.57 \\ 8.32 \end{bmatrix} \quad \mathbf{r}^* = \mathbf{T}^* \mathbf{1} = \begin{bmatrix} 3.69 \\ 4.30 \\ 3.12 \\ 4.62 \end{bmatrix}
\]

The elements are visualised and categorized by combining the corresponding values in vectors \( \mathbf{d}^* \) and \( \mathbf{r}^* \) as follows:
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- \( y = r^* - d^* \): is the “net position” of the risk items. A positive entry in \( y \) indicates that the corresponding risk item is predominantly a “dispatcher”, strongly influencing other risks. Whereas, if negative the item is predominantly a “receiver”, strongly influenced by other risks.
- \( x = d^* + r^* \): is the “total intensity” of the risk items. Similarly to the concept of weighted node degree in a network, larger-valued entries in \( x \) denote risk items of greater overall relevance, considered simultaneously as a dispatcher and receiver.

With reference to the data gathered for an actual respondent, Figure 4 (above) shows an alternative scatterplot of the same risk items according to their net position and total intensity indicators computed according to the DEMATEL procedure described above. In Figure 4, risks regarded as endogenous and environmental are shown with total intensity increasing from right to left (greyed area), whereas risks regarded as exogenous to the individual firm but endogenous to the PSC are shown with total intensity increasing from left to right.

**DISCUSSION**

Although derived from a limited respondent base, the results illustrated in the previous section already provide some structural insights into the propagation of risks in a generalised PSC when possible interdependencies between risks are explicitly taken into account.

Joint examination of Figures 3 and 4 leads to the following observations:

- **Dependent risks** (items falling in Quadrant III of Figure 3; bottom half of Figure 4) are mostly located downstream, reflecting a linear upstream-to-downstream flow of influence. For example, almost all the risk items included in the category “downstream engagement and demand fulfilment” exhibit high dependency (bottom-right quadrant in Figure 3; and bottom half of Figure 4). Most of these items are perfectly dependent (nil influence). Those items that more closely reflect the overarching PSC risk concept defined in the theoretical perspective section, namely R046 (“Product shortage prevents patient getting product”) and R040 (“Delays in delivery to patient”), exhibit the highest dependence in Figure 3. Whilst these items are still prominent in Figure 4, risks belonging to other categories, namely R008 (“Late or incorrect delivery of materials”) and R064 (“Loss of license to operate”) exhibit higher rank in terms of receiver net position and intensity;

- **Influential risks** (items falling in Quadrant I of Figure 3; upper half of Figure 4) belong to heterogeneous categories. The highest ranking risk in this segment, R033, is technological in nature and related to the increasing complexity of medicines portfolios. Most contractual/regulatory compliance risks, and risks in the category “responsiveness to catastrophic and extreme events” fall in this segment (upper-left quadrant in Figure 3; upper half of Figure 4);

- **Relay (unstable) risks** (Quadrant III in Figure 3; middle-right/left in Figure 4): the presence of seven items in the upper-right quadrant in Figure 3 suggests some instability in the system, although none of these items scores simultaneously as high in influence and dependence. Relay items are either endogenous to the firm or environmental in nature, including categories such as: process complexity/variability; forecast accuracy; and inability of supply;

- **Ambiguous risks**: some risks are located in close proximity to the x or y-axis in Figure 3, such as R067 (“Failure/inability to comply with regulatory change”) and R072 (“Product diversion e.g. product not being sold in target market in the presence of price differentials”). These risks are more difficult to categorize and require further analysis (Godet, 2007).

- **Independent risks** (Quadrant IV in Figure 3; close to the centre in Figure 4): Almost half (~46%) of the risk items evaluated falls into the “autonomous” category and hence could be dismissed, as they exhibit weak influence and dependence. For example, two downstream risks have neutral net position, with R045 (“Extended applicability of GDP to handling points in the distribution chain”) being perfectly autonomous (graphically positioned at the point of origin in Figure 3 and 4; and a disconnected node in Figure 2). While relevant in terms of risk
identification, these risks might not propagate as pervasively as others, rather, they can be regarded as mostly self-contained and hence not a priority. Preliminary findings such as those discussed above provided the grounds for an expert-panel discussion in a follow-up workshop. Visual analytics analogous to those shown in Figure 3 and 4 were presented to the participants through interactive dashboards on multi-user touch-screen surfaces to enable further interrogation and exploration of the data as part of a small-group learning activity.

From a mitigation strategy perspective, the analysis lends itself to network theories on contractual relationships and their implications for supply chain management (Kim, Choi, Yan, & Dooley, 2011). More specifically, proposed risk management for networked risks (54% of those identified in our study) would be informed by the identification of influential, informational dependent, and relational mediation characteristics of risks. For independent risks (46% in our study) conventional approaches to manage and mitigate risk such as those prosed by Chopra & Sodhi (2004) and Kumar et al. (2016) would remain appropriate and relevant.

From a computational standpoint, similarities and differences between MICMAC and DEMATEL and the visual-analytical insights they generate are rarely pointed out. Rather, either technique is chosen upfront by individual studies without acknowledging the other. This reflects a more general lack of comparative research on SM approach since seminal works such as Lendaris (1980). For similar reasons, only few works to date address the issue of assessing the reliability and validity of the results obtained through these techniques (e.g., Shieh & Wu, 2016).

CONCLUDING REMARKS
This paper has presented an approach for the evaluation of interrelated risks that could compromise a pharmaceutical supply chain’s ability to serve patients. The approach was developed in line with multi-method research, and it encompassed the elicitation of expert knowledge on risk events across the PSC; the development of an online gamification-enabled platform for experts to conduct pairwise-comparisons; and the use of structural analysis methods to categorize and prioritize risks based on their identified interrelationships. These steps have been illustrated throughout the paper with reference to some preliminary results gathered from actual survey responses with a focus on the UK pharmaceutical landscape. Feedback and validation of preliminary findings through industry experts’ engagement confirm the utility of the approach in determining risk category clusters where interdependencies elevate their consideration beyond the single instance in which they are normally evaluated.

While existing techniques are employed as part of the proposed approach, its novelty lies in the broader process of expert judgement elicitation, from the identification of a sector-specific universe of risks, through to the analytical evaluation of the possible interdependencies between the identified risks, and up to bringing the analytical insights gathered from individual respondents back to the group for discussion and validation. The proposed approach promotes the innovative use of gamification-enabled structural modelling, thus explicitly addressing the challenges of engaging experts in a potentially cumbersome data gathering process. The panel discussion provided initial feedback on the respondents’ overall experience with the data gathering process, visualisation of results insights on ranking. Overall, the MATRisk app was found to be easy to use, and serving its purpose of expediting a comparison process potentially involving 5,000+ pairs of items. An obvious limitation of the research presented in this paper is that it relies on preliminary results gathered from a limited set of respondents. However, similar works often present aggregated view through a single super-respondent, or are vague with regards to whether single or multiple experts are involved in a study. Other limitations include the absence of a consistent approach on assessing the reliability and validity of the results obtained through SM techniques. Addressing these limitations calls for further research on this topic.
ACKNOWLEDGEMENTS
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REFERENCES


### APPENDIX – LIST OF RISK ITEMS EVALUATED THROUGH THE MATRisk APP

<table>
<thead>
<tr>
<th>Item</th>
<th>Category (based on text analysis and judgment)</th>
<th>Top-level classification (literature)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R001, R002, R003, R004</td>
<td>Adequacy of supply base</td>
<td>Exogenous to the firm, endogenous to the network</td>
</tr>
<tr>
<td>R005, R006, R007, R008, R009, R010</td>
<td>Continuity and acceptability of supply</td>
<td>Exogenous to the firm, endogenous to the network</td>
</tr>
<tr>
<td>R011, R012, R013</td>
<td>Dependability of upstream assets/infrastructures</td>
<td>Exogenous to the firm, endogenous to the network</td>
</tr>
<tr>
<td>R014, R015, R016, R017</td>
<td>Adherence to procedures and protocols upstream</td>
<td>Exogenous to the firm, endogenous to the network</td>
</tr>
<tr>
<td>R018, R019, R020, R021, R022</td>
<td>Effectiveness and efficacy of production</td>
<td>Exogenous to the firm, endogenous to the network</td>
</tr>
<tr>
<td>R023, R024, R025, R026, R027</td>
<td>Dependability of assets/infrastructure</td>
<td>Endogenous</td>
</tr>
<tr>
<td>R028, R029, R030</td>
<td>Adherence to internal procedures and policies</td>
<td>Endogenous</td>
</tr>
<tr>
<td>R031, R032, R033, R034</td>
<td>Technological capacity, agility and flexibility in manufacturing</td>
<td>Endogenous</td>
</tr>
<tr>
<td>R035, R036</td>
<td>Forecasts accuracy</td>
<td>Endogenous</td>
</tr>
<tr>
<td>R037, R038, R039</td>
<td>Inventory visibility and traceability</td>
<td>Exogenous to the firm, endogenous to the network</td>
</tr>
<tr>
<td>R040, R041, R042, R043, R044, R045, R046</td>
<td>Downstream engagement and demand fulfillment</td>
<td>Exogenous to the firm, endogenous to the network</td>
</tr>
<tr>
<td>R047, R048, R049, R050, R051</td>
<td>Dependability of downstream assets/infrastructures</td>
<td>Exogenous to the firm, endogenous to the network</td>
</tr>
<tr>
<td>R052, R053, R054, R055, R056, R057</td>
<td>Adherence to procedures and protocols downstream</td>
<td>Exogenous to the firm, endogenous to the network</td>
</tr>
<tr>
<td>R058, R059, R060, R061</td>
<td>Responsiveness to extreme and catastrophic events</td>
<td>Environmental</td>
</tr>
<tr>
<td>R062, R063</td>
<td>Socially responsible business behaviour</td>
<td>Environmental</td>
</tr>
<tr>
<td>R064, R065, R066, R067, R068, R069, R070</td>
<td>Contractual and regulatory compliance</td>
<td>Environmental</td>
</tr>
<tr>
<td>R071, R072, R073, R074</td>
<td>Awareness of markets dynamics and competition</td>
<td>Environmental</td>
</tr>
</tbody>
</table>

*Full description omitted due to space constraints. Details available on request.