SCIENCE-BASED RISK
GOVERNANCE
OF NANO-TECHNOLOGY

RISK GONE

Draft guidelines regarding the quantification of macro-economic benefits

DELIVERABLE 3.3

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Abstract

This report contains draft guidelines regarding the quantification of macro-economic benefits of engineered nanomaterials. A macro-economic benefit analysis of ENMs is needed for multiple reasons. Primarily to ascertain the economic footprint of ENMs and their importance in the macro economy. This will allow policy makers to direct resources as required into ENM support and development. Knowing the economic scale is also important to regulators who need to gauge any impact that regulation might have on the industry. Willingness to Pay (WTP) is examined first. This approach is particularly effective when considering a specific product or product group and can capture risk, risk perception and the consumer price point for that product. The application domain can be individuals as customers or companies as customers. This problem with this approach is that the use case specificity does not lend itself to a generic appraisal of the economic benefits of engineered nanomaterials. Rather, a welfare economics approach can capture the utility to a customer as the aggregate societal benefit of engineered nanomaterials. The analogy with a welfare economics/Cost Benefit Analysis of climate change may be relevant. A lack of clarity surrounding risk is an ongoing problem but as risk assessment improves, a welfare economics is an appropriate methodological approach to quantify macro-economic benefits of nanomaterials. To be clear, in this report we are interested in the financial risk but this financial risk is a significant proxy for human health and environmental risk. Here, we select a relevant and appropriate use-case to determine the efficacy of reducing Healthcare Acquired Infections (HAIs) utilizing nanomaterial coated textiles. From this use-case, we develop a more robust methodological approach using a fixed effects panel test. Finally, using the use-case scenario we derive a general approach that can be applied and aggregated to a macro economics approach. We suggest that a WTP approach is appropriate for nano-enabled products but a welfare economics approach is the ideal, strategic approach to quantify benefits of nanomaterials. In the near term, an econometric approach is an appropriate economic approach but this should include risk parameters as they become available.

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List Of Abbreviations

AgNP	Silver nanoparticles
CAGR	Compound annual growth rate
CAUTI	Catheter-associated urinary tract infection
CBA	Cost Benefit Analysis
CBC	Choice-Based Conjoint
CDI	Clostridium difficile (C.diff.) Infection
CuNP	Copper nanoparticles
GDP	Gross Domestic Product
ENM	Engineered Nanomaterial
HAI	Healthcare Acquired Infections
MCA	Multi-criteria analysis
MRSA	Methicillin-Resistant Staphylococcus Aureus
RA	Risk Assessment
RDM	Robust Decision Making
RG	Risk Governance
RM	Risk Management
SSI	Surgical site infection
WTP	Willingness To Pay
ZnNP	Zinc oxide nanoparticles

1. Aims and Scope

Aims

The aim of this task and deliverable is the provision of draft guidelines that will facilitate the quantification of economic benefits of Engineered Nanomaterials (ENMs). The human and environmental risks relate to tasks 3.1, 3.2 and 3.4. The approach references and uses economic approaches such as Willingness-To-Pay (WTP) and the Welfare Economics Model.

Scope

The physicochemical properties of any one ENM can vary significantly and there are many multiples of ENMs being produced. The agglomeration of a nanomaterial in an end product, the production process, the exposure rate and exposure routes all have an impact on the risk to human and environmental health. Finally, the number products that already contain ENMs range from cosmetics to electronics from automobile manufacture to medical applications and thousands of other products.

The economics and societal benefits of ENMs must be weighed against the potential risks and this balancing act will come into acute focus if there is an occurrence of a real or perceived ENM risk. In that case, an overzealous regulatory response may have unintended economic consequences.

Given the complexity and variety of ENMs and their usage, there is no economic model that fits all instances and can be simultaneously practical. Therefore, flexible guidelines that can be used in a general case are intended to provide a robust methodological approach that can be adapted to a particular industry or sectorial instances.

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2. Introduction

ENM Economic Potential

Nanomaterials as defined in a 2011 Commission Recommendation (EU 2011), are materials which often have specific properties due to their small particle size.

The global market for nanomaterials is estimated at 11 million tonnes at a market value of €20 billion. The current direct employment in the nanomaterial sector is estimated at 300,000 to 400,000 people in Europe. It is still dominated by materials which have been in use for decades, such as carbon black (mainly used in tyres) or synthetic amorphous silica (used in a wide variety of applications including tyres, as polymer filler but also in toothpaste or as anticoagulant in food powders).

In the past years, many new nanomaterial-related applications have been developed. Those include a number of consumer products such as UV-filters in sun creams and anti-odour textiles. However, many medical and technical applications such as tumour therapies, lithium-ion batteries which can drive electrical cars, or solar panels also exist. Those applications have the potential to create major technological breakthroughs, and therefore nanomaterials have been identified as a key enabling technology. Products underpinned by nanotechnology are forecast to grow from € 9 billion in 2019 at a compound annual growth rate (CAGR) of 13.1% from 2020 to 2027 (GrandViewResearch 2020).

The RiskGONE project aims to contribute significantly to regulatory Risk Assessment (RA) of ENMs and to provide solid procedures for science-based inter-disciplinary Risk Governance (RG), based on a clear understanding of risks, risk management (RM) practices and the societal risk perception by all stakeholders, to allow the European Union (EU) to fully exploit the economic and social potential of ENMs and nanotechnologies broadly.

To address the gaps identified above regarding the RG of ENMs, RiskGONE's declared objectives are to:

> Establish mechanisms for bidirectional communication with stakeholders and civil society for managing possible nanotechnologies risks with regard to both social and environmental impacts while maximising the economic potential across the spectrum of application areas.

Economic Theory

There are two viable model approaches specified in the task description, Willingness-To-Pay and the Economic Welfare model. The following two sections detail those approaches. Later sections summaries these approaches as candidate guidelines to form economic guidelines that can be applied by the Risk Governance Council.

Willingness-To-Pay (WTP)

Willingness to pay (WTP) is the maximum amount an individual or company is willing to pay to obtain a product or service. If the transaction proceeds, the price negotiated will be between a buyer's willingness to pay and a seller's willingness to accept (Wertenbroch and Skiera 2002). At that price, the consumer is indifferent to buying or not buying, because WTP reflects the product's inherent value in monetary terms. That is, the product and the money have the same value, so spending to obtain a product is the same as keeping the money.

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As an economic approach to determining the additional cost a consumer or company is willing to pay for a nano-enhanced product, WTP is an appropriate methodology. The results allow manufacturers to gauge customer acceptance and can set a price premium based on the responses elicited.

WTP can be measured directly from individuals/companies through structured conversations or through a marketing questionnaire survey of a population sample. This can then be used as the basis for estimating aggregate WTP for the customer base. This approach, called 'contingent valuation,' is conceptually attractive because it potentially allows the analyst to elicit a WTP amount for impacts that involve both active and passive use.

The WTP method was first applied in the health area by (Acton 1973). WTP is interpreted as an indicator of how much personal satisfaction or well-being (often called 'utility') individuals derive from (or believe they derive from) different health outcomes.

Consumer surplus = WTP – actual payment (Welfare triangle). In a partial equilibrium market diagram, the Harberger triangle representing the net welfare benefit or loss from a policy or other change. In trade theory it often means the triangle or triangles representing the deadweight loss due to a tariff.

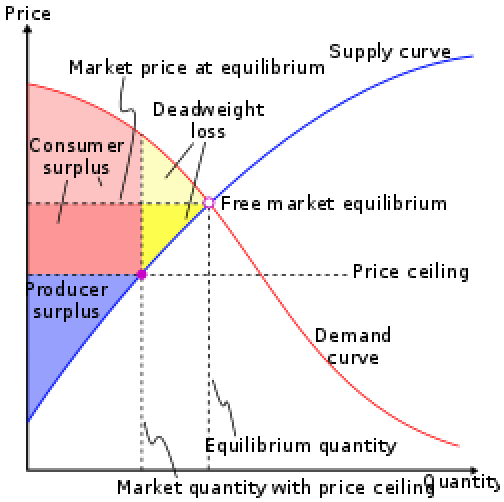

Figure 1 Deadweight loss created by a binding price ceiling. The producer surplus always decreases, but the consumer surplus may or may not increase; however, the decrease in producer surplus must be greater than the increase, if any, in consumer surplus.

Anderson, Jain, and Chintagunta (1992) demonstrate that consumers' WTP is "*the cornerstone of marketing strategy*". For clarity, in this context marketing includes pre-product launch period and refers more to market demand. First, customers' WTP is a key input for price response models that inform optimal pricing and promotion decisions. Second, a new product's price must be carefully chosen to ensure that any investment in development will be recuperated and profits made. This is key to avoid innovation failures (Ingenbleek, Frambach, and Verhallen 2013). Not only do companies need to know what consumers are willing to pay early in their product development process, but WTP is also of interest to researchers in marketing and economics who seek to quantify concepts such as a product's value (Steiner et al. 2016).

There are several approaches to the WTP model. It is first assumed that consumers want the most features at the lowest price. From the perspective of the producer this selection of feature is very dependent on the production costs. In our case this is likely to mean the

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inclusion, or otherwise, of a nanomaterial to enhance the feature or utility of the product. There are no ‘real control features’, so demand must be measured in a hypothetical sense with the customer asked a series of questions on their preference for various attributes they are likely to prefer.

There are multiple design approaches to a WTP model. The most popular is a Conjoint analysis. This approach permits a realistic evaluation of choices among hypothetical features that vary simultaneously: conjoint = “consider jointly”. The predominant form of this is so-called “Choice-Based Conjoint” analysis (“CBC”), where products are considered to be different combinations of features and price.

CBC analysis is popular method of product and pricing research that helps uncover preferences for product features, sensitivity to price, forecast market shares, and predict adoption of new products. Marketing use and application includes feature selection for new or revamped products, marginal WTP for specific features relative to other features, price elasticity of demand to understand how sensitive customers are to price changes, determining the optimal price for your products while taking into account competition, cannibalisation, customer preferences and testing branding, packaging and advertising claims.

The first step in a CBC analysis is the identification of product or service attributes. By defining products as collections of attributes and having the individual consumer react to a number of alternatives, one can infer each attribute’s (i) importance and (ii) most desired level for each consumer. Conjoint analysis provides a method to assess an individual’s “value system,” which specifies directly or indirectly the monetary value a consumer puts on each level of each of the attributes. If we know an individual’s value system, we can predict which of a set of available alternatives the individual might buy. The main idea in conjoint analysis is to construct the value system by asking about preferences on a small subset of products and then using the system to make predictions about relative preferences for any products that are plausible and could be sold in the market place.

Consider a simple example. A lipstick product has two attributes (i) a cost per product, €5 or €6 per stick (ii) a gloss effect mode using nanoparticles or not. So there are 2 x 2 cost combinations (or products). A questionnaire can query consumer preference by ranking the products in order of preference (preference 1 to 4) or ask the customer to describe the importance of the attribute. When the ranking or importance are assigned, utility points can be associated with each attribute allowing us to calculate aggregates, averages and so on, allowing us to compare a customer’s “value system” against peer responses.

A conjoint study has following six design stages.

1. Determine Relevant Attributes and their levels.

   In conjoint, the researcher must specify the attributes that influence customer decisions. These include

   a. Physical attributes - refers to the product itself, for example, product weight or size.

   b. Performance benefit - refers to outcome, for example, kilometres per litre.

   c. Cost-based attributes - refers to cost of acquiring the product or service or cost associated with continuing to use the service. This includes installation cost as well as monthly charges or fees.

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   d. Psychological positioning - refers to user perception, for example, assurance.

2. Determine Product Presentation: Content and Form.

In the full profile approach, each product is described in terms of all the relevant attributes. The alternative “partial profile” approach describes concepts on only a subset of the full attribute list. Partial profiles are often used when describing a product concept or when the full product attributes are too numerous to include.

3. Determine Respondent - Researcher Interaction format.

The responses can be obtained by interview, by phone or by internet. A mixed mode approach is also useful. Cost of implementation and sample size are the two competing problems in obtaining data.

4. Decide on Response Type, rating, ranking, or choice.

Customers can be asked to make decisions based on ratings or ranks or choices. In rating, without explicitly considering other options, customers were asked to state how likely they would consider purchasing an item. In ranking, customers are asked to rank products from most to least desirable. Choice allows the customer to pick from a number of choices or no at all.

5. Determine Criterion for judging, liking, purchasing or willing-to-pay.

Judgement or liking a product are quite different from willing-to-pay. A customer might like a Ferrari for €120,000 but are willing to pay €25,000 for a Nissan.

6. Decide on Data Analysis Technique.

The most common techniques are described below.

Form of Judgement about alternatives	***Data Analysis***
Rating Scores Regression Analysis	Rating Scores Regression Analysis
Probability of Purchase Logit Model	Probability of Purchase Logit Model
Rankings MONANOVA or LINMAP	Rankings MONANOVA or LINMAP
Choice Multinominal Logit	Choice Multinominal Logit
Share Allocation Share Model	Share Allocation Share Model

Table 1 – Common Analysis techniques based on form of judgement on a Conjoint Analysis.

In conjoint analysis, the individual provides details on their preferences or judgments and the individual value system is computed. Collectively, the responses can be analysed using an aggregate analysis of attribute importance, a segmentation analysis or a scenario simulations to predict demand levels.

The most common interpretation is to compute the average of each attribute level across the entire sample set of responses to show which attributes are generally important and their desired levels.

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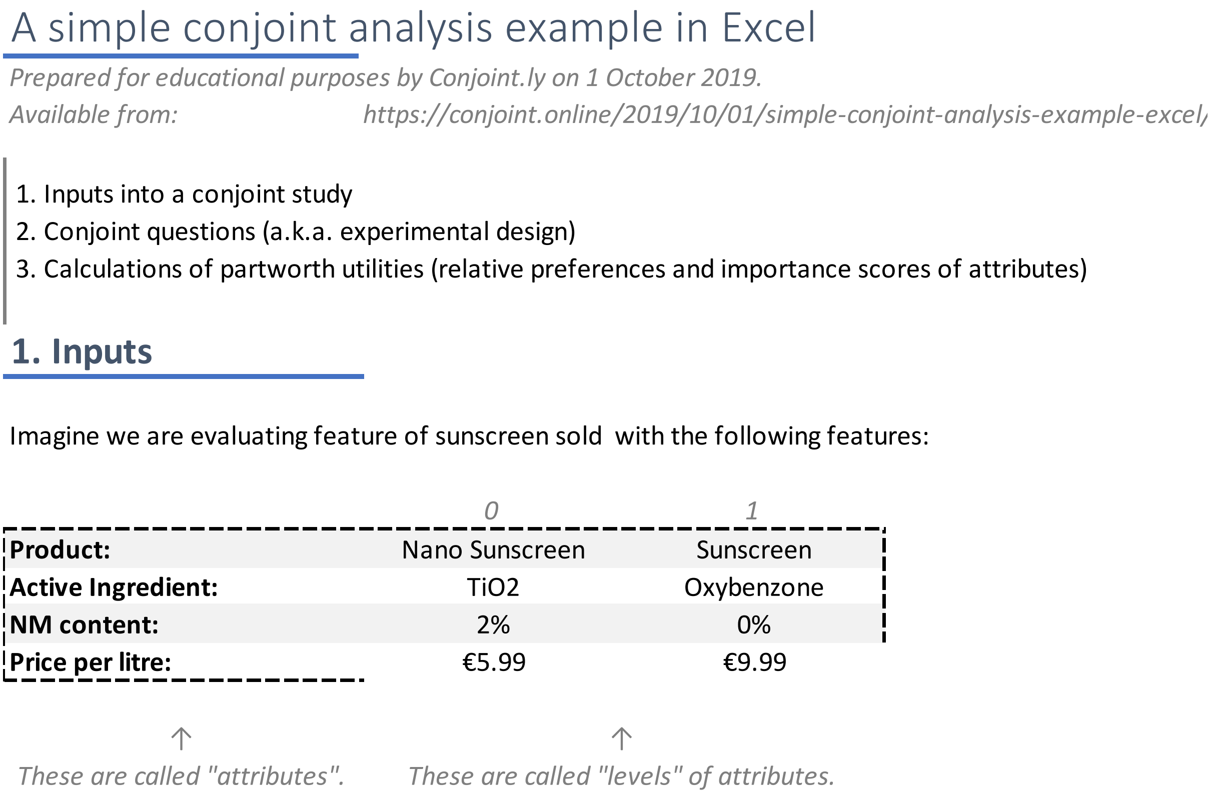
The segmentation analysis allows for the separation of different respondent classes and examining their preferences as a subgroup. This segmentation is based on predefined groupings, for example urban versus rural or segmenting for different social-economic classes.

Given the value system of a consumer and a description of alternative products, alternative products can be valued. This allows for the prediction of choices the consumer would make if confronted with alternatives in the market place.

In the following screenshots, we present a simple example of the use of a conjoint analysis in a WTP approach. The example is taken from a modified excel spreadsheet and we assume that a series of respondents are asked questions on their preferences regarding the purchase of sunscreen with TiO_2 nanomaterial as the active ingredient. There is also a price differential. In the example there are 4 attributes with two levels each. A more realistic WTP approach would have much more attributes and levels.

In Figure 2 below, the attributes and levels are specified.



A simple conjoint analysis example in Excel

Prepared for educational purposes by Conjoint.ly on 1 October 2019.

Available from: https://conjoint.online/2019/10/01/simple-conjoint-analysis-example-excel/

1. Inputs into a conjoint study
2. Conjoint questions (a.k.a. experimental design)
3. Calculations of partworth utilities (relative preferences and importance scores of attributes)

1. Inputs

Imagine we are evaluating feature of sunscreen sold with the following features:

	0	*1*
Product:	Nano Sunscreen	Sunscreen
Active Ingredient:	TiO2	Oxybenzone
NM content:	2%	0%
Price per litre:	€5.99	€9.99

↑ *These are called "attributes".*

↑ *These are called "levels" of attributes.*

Figure 2- A simple Willingness-To-Pay analysis. Conjoint Analysis (also called trade-off analysis) is used in many social science disciplines, including marketing, product management, and pricing. This excel example shows a conjoint analysis example.

In Figure 3 below, the consumer is asked to pick from a range of options. Each product is a combination of different levels. This will force participants to consider these levels and product jointly and make trade-offs between different products.

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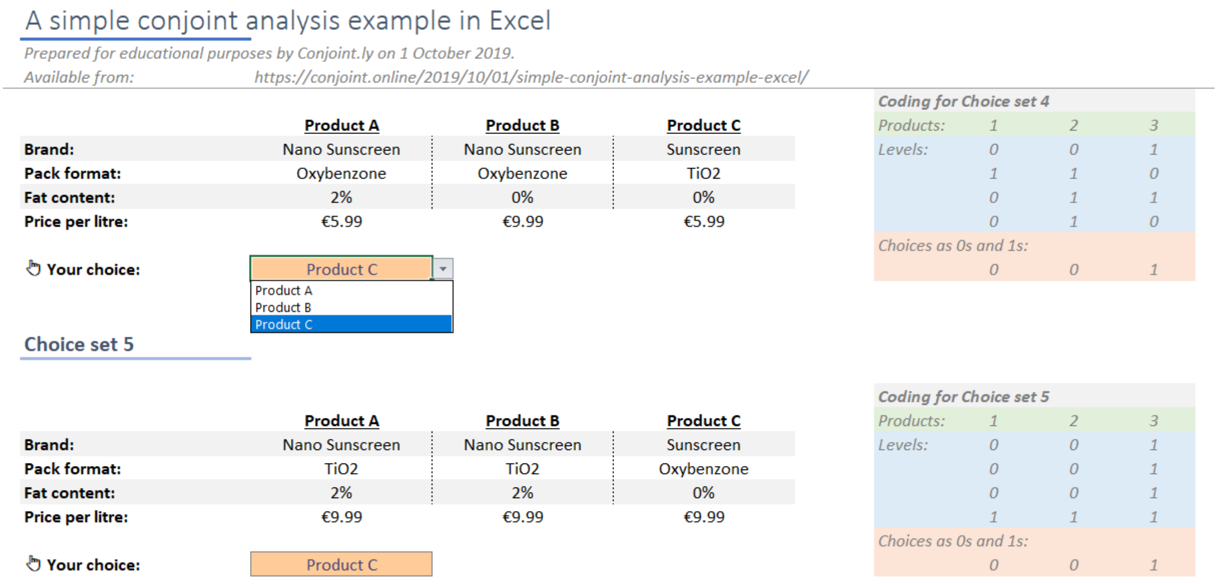


A simple conjoint analysis example in Excel

Prepared for educational purposes by Conjoint.ly on 1 October 2019.

Available from: *https://conjoint.online/2019/10/01/simple-conjoint-analysis-example-excel/*

	Product A	**Product B**	**Product C**
Brand:	Nano Sunscreen	Nano Sunscreen	Sunscreen
Pack format:	Oxybenzone	Oxybenzone	TiO2
Fat content:	2%	0%	0%
Price per litre:	€5.99	€9.99	€5.99

Your choice: Product C

Product A
Product B
Product C

Coding for Choice set 4			
Products:	*1*	*2*	*3*
Levels:	*0*	*0*	*1*
	1	*1*	*0*
	0	*1*	*1*
	0	*1*	*0*
Choices as 0s and 1s:			
	0	*0*	*1*

Choice set 5

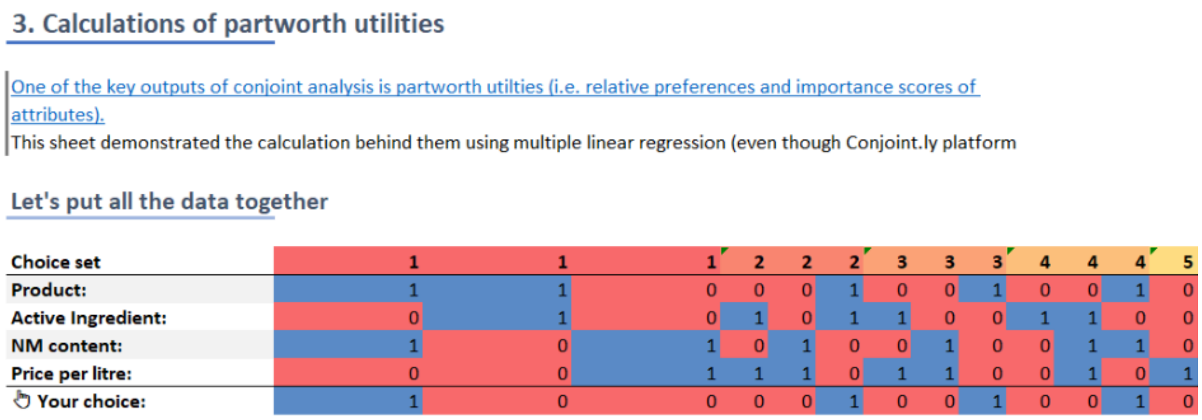
	Product A	**Product B**	**Product C**
Brand:	Nano Sunscreen	Nano Sunscreen	Sunscreen
Pack format:	TiO2	TiO2	Oxybenzone
Fat content:	2%	2%	0%
Price per litre:	€9.99	€9.99	€9.99

Your choice: Product C

Coding for Choice set 5			
Products:	*1*	*2*	*3*
Levels:	*0*	*0*	*1*
	0	*0*	*1*
	0	*0*	*1*
	1	*1*	*1*
Choices as 0s and 1s:			
	0	*0*	*1*

Figure 3 –The consumer is asked to pick from a series of options

The screen in Figure 4 demonstrates the calculation using multiple linear regression (although logit regression is more commonly used).



3. Calculations of partworth utilities

One of the key outputs of conjoint analysis is partworth utilties (i.e. relative preferences and importance scores of attributes).

This sheet demonstrated the calculation behind them using multiple linear regression (even though Conjoint.ly platform

Let's put all the data together

Choice set	**1**	**1**	**1**	**2**	**2**	**2**	**3**	**3**	**3**	**4**	**4**	**4**	**5**
Product:	1	1	0	0	0	1	0	0	1	0	0	1	0
Active Ingredient:	0	1	0	1	0	1	1	0	0	1	1	0	0
NM content:	1	0	1	0	1	0	0	1	0	0	1	1	0
Price per litre:	0	0	1	1	1	0	1	1	0	0	1	0	1
Your choice:	1	0	0	0	0	1	0	0	1	0	0	1	0

Figure 4 Data Set gathered

Figure 5 below shows the aggregated importance scores

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	Raw regression coefficient	Range	Importance score
Price per litre:	-0.16	0.16	17%
NM content:	-0.12	0.12	13%
Active Ingredient:	-0.03	0.03	3%
Products:	0.62	0.62	67%
Model intercept:	0.25		
Total		**0.93**	**100%**

Figure 5 – The calculated importance scores

Finally, we calculate the preference scores and show them in Figure 6 below.

		Raw regression coefficient	Centered coefficient	Preference score
Price per litre:				
	€5.99	0	0.08	8%
	€9.99	-0.16	-0.08	-8%
NM Content				
	2%	0.00	0.06	7%
	0%	-0.12	-0.06	-7%
Active Ingredient:				
	TiO2	0.00	0.01	1%
	Oxybenzone	-0.03	-0.01	-1%
Product:				
	Nano Sunscreen	0	-0.31	-34%
	Sunscreen	0.62	0.31	34%
Average			0	0%

Figure 6 – Preference Scores.

This simple example shows the relative ease of creating a WTP model and the implementation provides useful metrics on consumer product preferences. The same approach can be applied to a wholesale market where the customer is an end manufacturer of a product that contains or utilizes nanomaterials.

Welfare Model

Welfare economics is defined as a branch of economics that studies how the distribution of income, resources and goods affects the quality of living standards in an economy. An example of welfare economics is the study of how certain health services help bridge the barrier between different classes of people.

Economic welfare can be measured through a variety of factors such as GDP and other indicators that reflect the welfare of a population (such as literacy, number of doctors, levels of pollution etc). An increase in real GDP output and real incomes suggests people are better off and therefore there is an increase in economic welfare. However, economic welfare is concerned with more than just levels of income. For example, people's living

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standards are also influenced by factors such as levels of health care, and environmental factors, such as congestion and pollution. These quality of life factors are important in determining economic welfare.

Figure 7 below shows some of the factors that can be used to measure welfare economics. The top of the diagram shows empirical economic variables that can be observed from statistical data. The bottom half are somewhat intangible but can also be measured. For example, Life expectancy and quality of life can be measures by access to healthcare, lifestyle health, e.g. levels of obesity/smoking rates.

While economics is concerned with ideas of utility, welfare economics is devoted to determining the optimal allocation of resources in society. So, for orthodox economics, the allocation of efficiency and utility represents the satisfaction or happiness of a consumer. For example, if a person pays €2 for a bottle of water then, for that person, a utility of at least €2 is derived from that product.

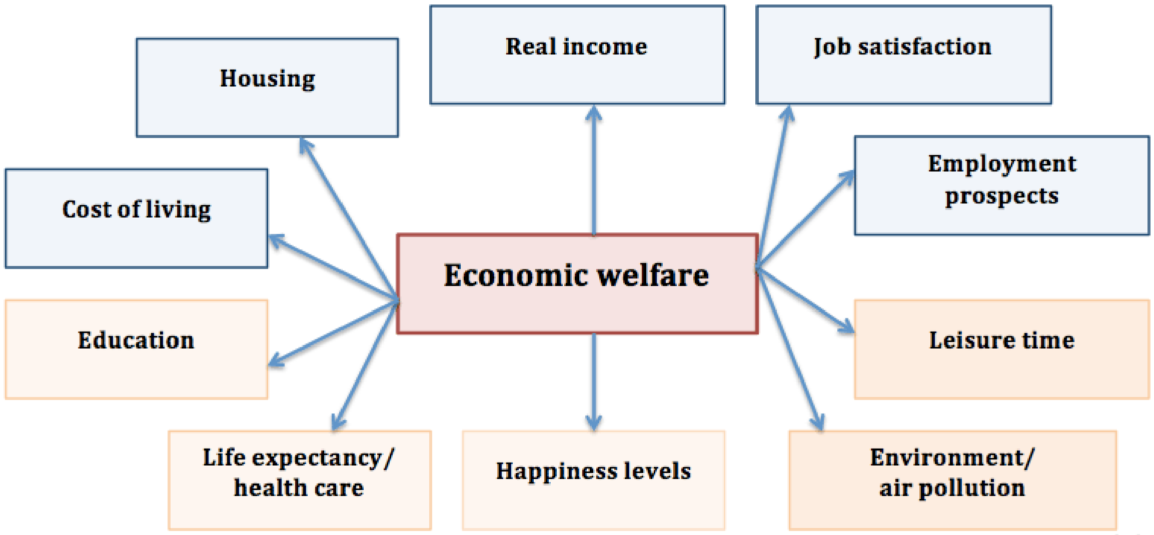

Figure 7- Factors influencing economic welfare. Source: www.economicshelp.org

There are two fundamental theorems of welfare economics. The first fundamental theorem is also known as the “Invisible Hand Theorem” and states that any competitive equilibrium leads to a Pareto efficient allocation of resources. This posits that markets in equilibrium lead to a social optimum. Thus, no intervention of the government is required, and it should adopt only “laissez faire” policies. However, in practice government intervention is normal and the conditions for this theorem to work are rarely seen in real life.

The second fundamental theorem of welfare economics states that any efficient allocation can be attained by a competitive equilibrium, given the market mechanisms leading to redistribution. This theorem allows for a separation of efficiency and distribution matters. Those supporting government intervention will ask for wealth redistribution policies.

There is a useful analogy here when comparing the efficacy and challenges of a Cost Benefit Analysis (CBA) of the use of nanomaterials to a related cost benefit analysis of climate change. Applying a CBA to climate change is challenging because of the nature of the science: how the climate system acts over time must be considered along with the ways in which natural and human systems are altered by, and respond to, these changes in climate. Further complicating the challenge are questions about how human and natural

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systems will evolve during the long time frame over which climate policies are analyzed, including factors such as changing preferences, changing incomes, and the cost and availability of technologies to mitigate climate change or respond to its impacts (Sussman, Weaver, and Grambsch 2014).

Sussman, Weaver, and Grambsch (2014) identify five characteristics of the climate system and associated impacts on human and natural systems that pose particular challenges to CBA of climate change. The identified challenges can be equally applied to nanomaterials

1. ubiquity of impacts

   Ubiquity of impacts manifest on both a positive and negative basis. Negative impacts may include occupational health for workers or environmental damage. There can also be time related impacts where a malign event might not manifest itself for several years. On the positive side, it is difficult to list and therefore measure the positive impacts. Product utility has and is improving from clothing to vehicle tyres to electronic devices. Nanomedicine has shown great promise in terms of drug delivery and other aspects of human health improvements. Water filtration systems are equally promising. The ubiquity of positive impacts cannot be captured by a simple number such as “the value of the nanomaterial industry”. That said, in this report we present a case study in the area of ENM coated hospital textiles and go on to develop guidelines showing how this can be applied more generally. Eventually, a broad based effort can lead to a quantification of revenue growth, job creation and risk costs.

2. Intangibility

   Intangibility refers to the difficulty or impossibility of measuring a product improvement or increase in functionality. For example, a product may offer intangible benefits in human health. Societal health care cost reductions can be measured but there are larger societal benefits that are difficult to measure, for example well-being or mental health. Again, a case by case study can identify intangible benefits of ENM applications. This report delves into a one such case study and presents guidelines on how this can be applied more generally.

3. Non-marginal changes

   Changes in quantity being evaluated are too small to affect market prices. The applicability of most measures also relies on assuming *ceteris paribus*: incomes, prices in other markets, the structure of the economy, and other factors affecting values remain unchanged during the time frame of the analysis. In other words, the multiple incremental changes ascribed to nanomaterials across all industrial sectors are vital in the aggregate but difficult to capture individually.

4. Long timeframes

   Generally, the timeframes of the economic benefits of nanomaterials can be assessed with some degree of accuracy. This is especially true when examining use cases as this report does. However, the uncertainty of the risk of nanomaterials poses a long timeframe problem. For example, if a particular nanomaterial is found to have negative human or environmental outcomes, these may present themselves over a long timeframe or tail risk in the parlance of insurers. An oft cited example is asbestos which continues to pose a hazard to human health.

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5. Uncertainty

   Finally uncertainty is an economic impediment. The risks posed by nanomaterials, be they real or perceived, can act as a brake on research and investment.

These characteristics interact with traditional economic challenges, such as valuing non-market impact, addressing non-marginal changes, accounting for low-probability but high-impact events, and the difficulty of appropriately discounting the future.

In summary, WTP and Welfare economics both possess useful characteristics for decision makers. WTP can and should be used for a specific product or product class. However, its usefulness to decision makers beyond a specific product group is questionable. Welfare economics has greater potential. We feel the analogy with of a Cost Benefit Analysis of climate change is apt. However, similar hurdles are faced, in particular, a reduction of the risk uncertainty of nanomaterials is required. With improving methodologies a CBT/Welfare Economic approach certainly has significant potential.

In the interim, a more orthodox and practical approach is required. To that end, in the next section, we delve into a specific use-case and in the following section extract useful methodologies from that use-case for a more generic approach to economic modelling.

3. Use Case Selection

Criteria

The title of Work Package 3 in the RiskGONE project is Guidelines for Risk Benefit Assessment. T3.1 will deliver draft guidelines for risk assessment in M36. T3.2 will produce draft guidelines regarding the quantification of lifecycle environmental and human health risk indicators in M21.T3.7 will, with available data, utilize the draft guidelines in selected ENM case studies for evaluation. The overall work package will present draft guidelines regarding bringing together risk indicators in an overall MCA framework.

This context is important because this report will feed the final WP deliverable. In that context, while the T3.7 will prepare case studies for evaluation, the economic guidelines will precede the case studies. However, in developing the economic guidelines, a standalone case study was selected in order to develop the economic guidelines. To be clear, the case study picked in this task only serves a specific purpose (economic guidelines) and it is not necessary to integrate the WP case studies.

With this in mind, a suitable case study that incorporates and develops a pressing social problem, occupational and environmental risk along was selected. Namely, the use of Engineered Nanomaterials (ENM) in a healthcare or hospital setting. ENM coated textiles have demonstrable anti-microbial properties and the technology to embed the ENMs in textiles has matured over the past five years to the extent that there are multiple research papers showing their efficacy in reducing Healthcare Acquired Infections (HAIs). HAIs are a persistent problem, particularly in acute hospitals and are the cause of additional mortality rates in both developed and developing economies. Despite significant progress in reducing HAI rates, particularly with hand hygiene, HAI infections still occur in about 7% of hospital stays. Notwithstanding the human cost in terms of death and suffering, the economic costs of the additional hospital stays amount to billions of euros annually.

There is ample clinical and nanomaterial research yet there is a significant absence of extant literature describing the economic cost benefit analysis of deploying ENM costed textiles in a

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widespread manner. The possible risks human and environmental risks of ENMs, particularly metal ENMs are also present in the manufacturing process, in the use of the materials in a hospital ward and in the washing and disposal of the materials. The potential for ENM coated materials to significantly reduce HAI incidence has significant economic potential and a significant 'social good' potential.

For all these reasons, we choose the economic benefit of using ENM coated hospital textiles as a case study. This is not without criticism. The applicability of one use-case economic setting is, for sure, difficult to apply to another disparate sector. For example, how can the economic modelling for ENM coated materials in hospitals be applied to ENMs utilized in fuel cells or food packaging. . In this report, we argue that choosing a complex use case is important but extrapolating the result to form generic guidelines should be the focus.

In this report, we apply the use case in a scaffold type approach. First, we compare the *economic* efficacy of using ENM coated hospitals against the standard practice of using antiseptic measures. We were not supposing an either/or scenario but comparing the economic justification for including ENM coated textiles as part of a hospital managers holistic approach to HAI reduction. In the course of our research, we published an article in *Nanomaterials* detailing our findings. This paper is largely presented in Section 4 ENM Coated Hospital Textiles.

Murphy, Finbarr; Tchetchik, Anat; Furxhi, Irini. 2020. "Reduction of Health Care-Associated Infections (HAIs) with Antimicrobial Inorganic Nanoparticles Incorporated in Medical Textiles: An Economic Assessment." Nanomaterials 10, no. 5: 999.

The next stage in the scaffolding process is to follow this research with a more robust analytical approach. In section 5 we detail how the scenario can be developed to provide a much more advanced, albeit case-study specific approach. In this section we use a fixed effects regression approach.

In section 6, based on the preceding sections, we develop generic economic guidelines that can be utilized in all use case settings.

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4. ENM Coated Hospital Textiles

Introduction

Healthcare associated infections (HAIs) are infections that acquired while receiving health care in a hospital or other health care facility that first appear 48 hours or more after hospital admission(Mayhall 2012) or within 30 days after discharge following in patientcare(Revelas 2012). In the US, is has been reported that HAIs are the most common complications of hospital care and one of the top 10 causes of death(AHRQ 2018). The overall direct cost of HAIs to hospitals in the US ranges from USD 28 billion to 45 billion(Stone 2009). In the EU, it is estimated that 6.5% of patients in acute care hospitals had at least one HAI (Suetens et al. 2018). Hospital related costs in Europe are estimated at $12 billion per year(Solomon 2016). In Australia the burden of HAI has been calculated to be approximately 165,000 cases per year, rendering them the most common complication for hospital patients (NHMRC 2019; Higgins and Green 2011). Given their huge costs, the World Health Organisation has been leading efforts to formulate and publish Clinical guidelines and interventions in an effort to decrease the incidence of HAIs(WHO 2016).

The most common sources for HAIs are person-to-person transmission, medical equipment or devices, ventilator-associated pneumonia(Soussan et al. 2019), healthcare personnel, contaminated drugs and food. Medical textiles are considered one of the possible vehicles of transmission(Fijan and Turk 2012). To address this risk, current guidelines by the Centre for Disease Control and Prevention (CDC) include appropriate washing of hospital textiles (i.e. collecting, sorting, transporting, laundering with appropriate water temperature, type of detergents, disinfectant, rinsing and finishing, drying and ironing), but also their disinfection and in certain cases even sterilization. These procedures are effective but subject to continuous and rigorous implementation. Moreover, there are evidence of microorganisms survival on medical hospital textiles after laundering(Wilcox and Jones 1995), though the literature in the field is confusing and even contradictory. Against this backdrop, the use of antimicrobial inorganic ENMs incorporated in medical textiles is among the most promising strategies to provide aseptic conditions in hospitals(Pelgrift and Friedman 2013). Some Engineered Nanomaterials (ENMs) have proven anti-microbial properties that are particularly effective at the nano scale in contrast to their bulk form ENMs. In particular copper and silver oxide nanoparticles and nanoclays, are already used in food packaging(Bumbudsanpharoke, Choi, and Ko 2015) and food preservation(Bajpai et al. 2018). The anti-microbial properties of some ENMs have encouraged significant research in their application in health science. In contemporary settings, ENMs have found multitudinous applications in healthcare environments to reduce the incidence of infections. In that vein, instances of ENMs incorporated into medical textile has grown significantly over the last decade. In order to justify the use of ENMs embedded medical textiles and to achieve a large scale implementation of them, a benefit-cost analysis is warranted. Arguably, the application of ENMs embedded medical textiles should not only prove economically justifiable, it also need to comparable to in terms of (cost) effectiveness to traditional routines to reduce the incidence of infections.

Traditional routines to reduce the incidence of infections include thorough cleaning using health care antiseptics, personnel hand washes and antiseptics, surgical hand scrubs, patient preoperative and preinjection skin preparations, etc. These are widely regarded as the most effective means to reduce HAI incidence. However, evidence shows that effective cleaning is not always implemented. In many studies, researchers marked high-contact surfaces with a ultraviolet marker to determine if those surface areas were subsequently

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cleaned(Carling, Parry, Rupp, et al. 2008; Carling, Parry, Von Beheren, et al. 2008). Carling et al. (2006) found that after routine cleaning only 47% of the surfaces had actually been cleaned sufficiently. Moreover, there seems to be a lack of compliance with hand hygiene protocols(Sax et al. 2009). The gold standard method for monitoring hand hygiene compliance is direct observation however this audit method is less than optimal. Studies have pointed out the advantages of electronic monitoring systems, yet, their cost effectiveness has not been determined. Armellino et al. (Armellino et al. 2012) describe a cost of $50,000 USD for the installation of an electronic monitoring system for a 17 bed intensive care unit yet, they do not report the cost associated with ongoing real-time feedback.

The conventional approach to HAI reduction has, arguably, reached something of a plateau. This suggests that antimicrobial ENM coated surfaces can represent an orthogonal approach with significant promise. ENMs can be used on hard surfaces but also on upholstery and fabrics. The active ingredient is usually copper nanoparticles (CuNP) and silver nanoparticles (AgNP) although there are other options such as Zinc oxide nanoparticles (ZnNP). These nanoparticles kill pathogens when they oxidize and release ions, which enter the bacteria membrane and destroy the pathogen. Metal nanoparticles are more powerful than their bulk form because their large surface area relative to their mass increases the number of ions released. Furthermore, the nanoparticles can continue to reduce the microbial burden almost perpetually(Grass, Rensing, and Solioz 2011).

We focus on textiles as they are an excellent substrate for bacterial proliferation and textiles are considered a transmission vehicle(Fijan and Turk 2012). This is particularly true when in contact with human skin. The natural secretions and desquamation provide the excellent moisture and temperature conditions for pathogens. The textile itself has a very large surface area, again, providing an excellent environment for bioburdens. Studies have shown that healthcare fabrics (sheets, pyjamas, uniforms, etc.) can contain heave microbial burdens(Neely and Maley 2000; Wiener-Well et al. 2011; Kramer and Assadian 2014). Indeed, pathogens can survive for weeks on textiles and even after an industrial wash cycle(Koca et al. 2012; Kramer and Assadian 2014).

Another reason for our focus on textiles is that their properties as an ideal substrate for pathogens make them also difficult to clean using traditional antiseptics except through a conventional wash cycle. Indeed, textiles such as uniforms, allow the pathogens to be transported from patient to patient. Similarly, movement of textiles such as bedsheets and curtains can aerosolize the pathogens present on the fabric. All told, ENM coated textiles represent a discrete new front in HAI reduction strategies.

It is clear that a multifaceted approach to HAI reduction that includes training, procedures, health care antiseptics, hydrogen peroxide vapour, and ultraviolet light along with self-cleaning surfaced using ENMs is required (Chemaly et al. 2014). However, there is a trade-off between a reduction of HAIs and the allocation of finite resources to implement those reductions. Both the health care antiseptic and ENM coated textile markets are witnessing significant growth period however their absolute and relative performance are largely undetermined due to the fact that, there are currently no randomized controlled trials of the efficacy of these systems in preventing HAIs(Boyce 2016). Given this deficiency, some studies offer a cost effective/benefit approach to guide decision making(Everett, Sitton, and Wilson 2017; Henson et al. 2014). In this article, we aim at closing a gap in current knowledge by specifically examining the economic efficacy of using antimicrobial ENMs incorporated in medical textiles. More specifically, we compare the economic advantage of

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health care antiseptics with that of textiles coated with ENMs. To be clear, we are not supposing that a binary choice should be made between health care antiseptics and textiles coated with ENMs, it is safe to assume that these two methodologies are complementary in their applications. Yet, this research does provide guidance on the difficult choice faced by health care administrators and clinicians in allocation economic resources to reduce incidence of HAIs, by examining to which extent textiles coated with ENMs can be considered at a level playing field with health care antiseptics. Due to a lack of detailed data at a ward level, we use an aggregate data framework, a modified approach of Schmier et al. (Schmier et al. 2016).

The objective of this article is to gauge the economic benefits afforded by the use of ENM coated textiles. A stand alone cost benefit analysis is not practical because there is insufficient data to make a determination. We use a relative comparison analysis to compare the economic effectiveness of ENM coated materials against a standard antiseptic approach. The results can assist in the administrative decision to utilize ENM costed textiles in healthcare settings.

For the remainder of this article, we first examine the relevance of HAIs and their economic consequences, particularly in Europe. We then examine the prevalence and use, cost and effectiveness of both antiseptics and ENM coated textiles to set up a comparison. The next section introduces our methodology. This is followed by detailed results and an associated discussion. Before offering a conclusion, we offer some insights on how a regulatory approach would impact the current environment.

Healthcare-associated infections (HAIs)

Healthcare-associated infections (HAIs) are defined as infections occurring in a patient during the process of care in a hospital or other health care facility which was not present or incubating at the time of admission(WHO 2020). HAIs also referred to as "nosocomial" or "hospital" infections. The European Centre for Disease Prevention and Control (ECDC) estimate that, on any given day, about 80 000 patients, or one in 18 patients, in European hospitals have at least one healthcare-associated infection (Zarb et al. 2012). The most frequent types of HAI are surgical site infections, urinary tract infections, pneumonia, bloodstream infections and gastrointestinal infections. About 7% of patients in acute care hospitals in Europe experience a HAI. The documented range of HAI's per patient is 3–10% across EU member states with an average rate of 7%(EASAC 2009). MRSA (Methicillin-resistant Staphylococcus aureus) infections are the most common and increase the hospitalization period from an average of 4 to 14 days with additional costs varying from €10,000€ to €36,000 per patient (Stone, Larson, and Kawar 2002; Kim, Oh, and Simor 2001). The annual mortality directly attributable to nosocomial infections is estimated to be about 37,000 in the EU but this number could increase to 110,000 if indirect deaths are counted(EASAC 2009).

There is a clear evidence between the incidence of HAIs and the environmental microbial contamination present in health care setting (Goodman et al. 2008; Eckstein et al. 2007). Furthermore, common nosocomial pathogens may persist on surfaces for months providing a continuous source of microbial transmission (Kramer, Schwebke, and Kampf 2006; Kramer and Assadian 2014). These hard and soft surfaces in clinical settings serve as a persistent source for nosocomial pathogens, that can be transmitted through contact and aerosolized particles with either direct transmission (patient touching contaminated surfaces) or indirect

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(hospital personnel may contaminate themselves by touching contaminated surfaces and subsequently transfer the microorganisms to the patients).

Aggressive measures have been introduced over the past several years to reduce the incidence of HAI. These measures include improved staff training, better disinfection and hygiene regimes and patient monitoring and isolation of infected patients. Specialist infection control staff, disposable equipment and antibiotic control programmes have also contributed. Despite these improvements, it appears that the conventional approach to HAI reduction has reached something of a plateau and there is a need to consider the use of additional measures and modern technologies to reduce patient hospitalization and concurrent costs. New technologies fall into several categories such as: (1). new liquid surface disinfectants (e.g. improved hydrogen peroxide liquid disinfectants), (2). improved methods for applying disinfectants (e.g. Microfiber cloths or mops and ultra-microfiber cloths for applying liquid disinfectants to surfaces), (3). self-disinfecting surfaces (e.g. coating surfaces with heavy metals such as copper or silver) (4). light-activated photosensitizers (e.g. nanosized titanium dioxide to surfaces and using UV light to generate reactive oxygen species that can disinfect surfaces), and (5). no-touch (automated) technologies (e.g. aerosolized hydrogen peroxide, hydrogen peroxide vapor systems, gaseous ozone, chlorine dioxide, saturated steam systems)(Boyce 2016).

Among the third category, active antimicrobial surfaces and fabrics represent a novel and effective approach to reducing the bacterial burden in clinical settings, especially those surrounding the patients. In particular, within medical environments, surfaces containing copper or copper oxide and silver have been found to reduce bioburden and the transmission of nosocomial pathogens (Mikolay et al. 2010; Salgado et al. 2013; Schmidt et al. 2012; Monk et al. 2014; Lazary et al. 2014).

Despite the enthusiasm and potential for ENM coated surfaces, particularly textiles, a significant understanding of the relative cost effectiveness of ENM coated surfaces is elusive. That is, ENM coated textiles have a demonstrated capacity to reduce the incidence of HAIs but this comes at an economic cost which is not necessarily justified when compared to existing HAI reduction techniques. To better answer this question, in this article, we examine the economic benefits of deploying ENM coated textiles against the use of health care antiseptics. The answer will allow healthcare administrators better allocate funding resources to optimize HAI incidence.

Health Care Antiseptics

The global antiseptics and disinfectants market size was valued at USD 16.75 billion in 2018 and is expected to grow to USD 28.1 billion by 2026, an CAGR of 6.7% (GrandViewResearch 2019). The high incidence of HAIs and their consequent costs and the increasing awareness of hygiene is driving demand. Medical device disinfectants, enzymatic cleaners and surface disinfectants are the three main types of prevailing disinfectants. Yet, evaluating their efficacy in reducing HIA cases and costs is challenging.

Schmier et al. (Schmier et al. 2016) provide interesting research on the economic savings associated with the use of hospital antiseptic products on preventable HAIs. In their paper, they show that antiseptic usage reduces HAI incidence and shows a cost saving of up to USD 4.25 million annually in the US alone. Schimier et al. use a simple approach that first

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examines the total number of HAI's, reduces that by the amount of preventable HAI's and reduces that further by those HAI's prevented by antiseptics.

Using antiseptic as a baseline HAI control means, we employ a modified version of Schmier et al.'s (2018) approach to determine the HAI reduction achieved by ENM coated hospital textiles.

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ENM Coated Hospital Textiles

The global value of the medical textile market was valued at USD 12.2 billion in 2018 and is expected to reach USD 18.5 billion by 2025 (360MarketUpdates 2019). Medical textiles can include surgical gowns, gloves, drapes, facemasks, dresses, and linens, which could be disposable or reusable based on the use-case. Overcash (2012) shows that factors such as cost, protection, and comfort are reasonably similar between disposable and reusable gowns and drapes but reusable surgical textiles offer increased sustainability benefits over similar disposable products in energy (200%–300%), water (250%–330%), carbon footprint (200%–300%), volatile organics, solid wastes (750%), and instrument recovery.

Antimicrobial textiles typically use copper, silver or a combination as the active agent though Zinc Oxide has also proven effective (Argirova M and Perelshtein 2017) in a burns unit. Table 2 below shows a summary of some of the research on HAI reduction by antimicrobial textiles in a healthcare setting.

Authors	**Result**	**Type**
(Lazary et al. 2014)	24% reduction in HAI per 1000 hospital days and a 27% savings in costs	Copper oxide impregnated linens
(Sifri, Burke, and Enfield 2016)	76% aggregate reduction in HAI	copper-impregnated composite hard surfaces and linens
(Marcus et al. 2017)	29% reduction in antibiotic treatment initiation events (ATIEs)	copper oxide-impregnated textiles
(Burke and Butler 2018)	28% reduction in total Clostridium difficile and multi drug resistant organisms MDRO.	copper-impregnated composite hard surfaces, bed linens and patient gowns
(Butler 2018)	37% reduction of HAI Clostridium difficile and MDROs	copper oxide-impregnated linens
(Petkova et al. 2014)	48% and 17% reduction of Staphylococcus aureus and Escherichia coli, respectively	Zinc Oxide (ZnO) nanoparticles with chitosan

Table 2 –Example papers showing a reduction of bioburden by antimicrobial textiles

It should be noted that Madden, Heon, and Sifri (2018) showed no significant reduction in incidences of healthcare facility-onset Clostridium difficile infection or MDRO acquisition when copper impregnated linen was used in a 40-bed long-term acute-care hospital.

Reducing the surface bioburden is an effective strategy to reduce HAIs (Mikolay et al. 2010; Salgado et al. 2013; Schmidt et al. 2012). The inherent biocidal properties of substances such as silver and copper surfaces offer an advantage to conventional cleaning, as the effect is continuous rather than episodic. For example, (Salgado et al. 2013) showed a 58% reduction in the rate of HAI when patients stayed in intensive care unit (ICU) with copper alloy surfaces.

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In addition to copper oxide particles, silver nanoparticle (AgNP) and AgNP/reduced graphene oxide (rGO) nanocomposite demonstrate antimicrobial activity against HAIs. (Noor et al. 2019)

Methodology

Our approach uses a modified version of the methodology proposed by Schmier et al. (Schmier et al. 2016) where they propose an antiseptic cost-benefit analysis. They identified five HAIs of interest (catheter-associated urinary tract infections, central line-associated bloodstream infections, gastrointestinal infections caused by Clostridium difficile, hospital- or ventilator-associated pneumonia, and surgical site infections). They then employ four initial inputs. First, the national estimates of the number of cases of each type of HAI. Second, the proportion of those HAIs that are preventable. Third, the proportion of preventable HAIs that can be prevented by the use of antiseptic or disinfectant. Fourth and finally, the average hospital cost incurred by each HAI. They gather these figures from published literature and aggregate the data. Their final result estimates the range of low and high estimates of annual HAI cases avoided through use of health care antiseptics at 12,100 and 223,000 respectively. Their estimate of the associated economic costs is USD 142 million and USD 4.25 billion, respectively.

One drawback of this approach is that the cost of the antiseptics used, and the cost of their application, is not included in the cost benefit analysis. Another drawback is the evident scale of the uncertainty in the results as well as the inability to control for other factors that could affect HIA prevalence and avoidance. We develop this model by estimating the cost associated with the purchase and application of the antiseptic solution. We then apply a similar approach for the purchase and use of ENM coated textiles. Whilst the cost-benefit analysis of both antiseptics and ENM coated textiles contain high uncertainty, by comparing the *relative* cost-benefit analysis, we argue that the respective variability is less concerning.

$$H \times P \times SP_T \times B_T - C_T \qquad (1)$$

Equation 1 above shows the Cost Benefit model of antiseptics. H is the annual total number of HAI incidence in the EU, P is portion of the preventable number of HAIs and SP_T is the portion of preventable HAIs due to antiseptics. B_T is the average economic cost of a patient suffering a HAI event. Finally, C_T is the cost of the antiseptic treatment, which includes the purchase and application of the antiseptic.

$$H \times P \times SP_E \times B_T - C_E \qquad (2)$$

Equation 2 above shows the same Cost Benefit model but applying ENM coated textiles as the unit of analysis. SP_E is the portion of preventable HAIs due to ENM coated textiles and C_E is the cost of the ENM coated textiles.

Finally while Schmier et al. (Schmier et al. 2016) use US data, this article uses EU data. Aggregate incidence rates of HAI in the EU are similar to those in the US and, to an extent, can be used as a proxy for results in the US and vis a versa.

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Results and Discussion

Total Number of HAIs

In 2016 and 2017, the European Centre for Disease Control (ECDC) coordinated site surveys to collect data on HAIs in hospitals and long-term care facilities in EU/EEA countries(Suetens et al. 2018). Depending on the nature of the HAI, the infection can be mild or severe and increases patient hospitalization and hospital costs. HAIs in hospitals alone cause more deaths in Europe than any other infectious disease under surveillance at ECDC.

A total of 8.8 million HAIs were estimated to occur each year in European hospitals and long-term care facilities combined. HAIs in hospitals (for example pneumonia, surgical site infections and bloodstream infections, are usually more severe than HAIs in long-term care facilities (for example respiratory infections other than pneumonia, urinary tract infections and skin and soft issue infections).

Proportion of HAIs that are preventable

An important *economic* question is whether zero incidents of HAIs is an optimal solution. According to a positive economic perspective, equating marginal utility with marginal cost incurred by expenditure to prevent HAIs, may not result with zero HAIs being the social optimum. However, it appears that even if zero incidents of HAIs were an optimal solution, preventing all HAIs is not possible. According to Umscheid et al. (Umscheid et al. 2011) between 55 and 70% are reasonably preventable which would equate to between 1.1 and 1.4 million avoidable infections and 49,500-63,000 avoidable deaths annually in the US. The financial costs associated with these potentially preventable infections are estimated to be as high as $23 billion USD per annum. Harbarth et al. (Harbarth, Sax, and Gastmeier 2003) reviewed 30 reports and estimated that 20% of HAIs are preventable but in their review found that between 10% and 70% prevention rates are reported. More recently, Gastmeier et al. (Gastmeier et al. 2010) report that 20 to 30% of HAIs in Germany could be preventable primarily through improved adherence to hygiene recommendations and optimisation of procedures. In either case, the implementation of comprehensive, evidence-based prevention strategies will tend to increase the prevention of HAIs but since resources are limited, an economic guideline needs to be utilized in order to optimally allocate scarce resources

Clearly, the proportion of HAIs that are preventable is context specific, and depends on the infection type and infection location along with the application of prevention procedures. In this study we use a range of values, 15%, 25% and 35% as appropriately conservative prevention estimates.

Prevented Cases due to Antiseptics

We are not aware of research that specifies prevention by antiseptic and by pathogen. We further assume aggregate prevention based on overall incidences of HAI rather than specific pathogen types. Several studies, notably Gordin et al (Gordin et al. 2005), examine the effectiveness of disinfectants on HAI pathogens. Aboualizadeh et al (Aboualizadeh et al. 2017) showed the effectiveness of disinfectants, namely ethanol, isopropanol, sodium hypochlorite, triclosan and triclocarban on MRSA pathogens. These (and many other studies) show the high effectiveness of antiseptic cleansers. On the other hand, the application of the disinfectants by hospital staff can be less than optimal. This is most clearly

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evidenced by (Pittet et al. 2000) paper on the effectiveness of a hospital-wide programme to improve compliance with hand hygiene.

In line with Schmier et al (Schmier et al. 2016), as a proxy for prevented cases due to antiseptics, we use a range of values of 10%, 20%, and 30%, not based on specific study but a conservative reflection of estimates in the literature.

Prevented Cases Due to ENM Coated Textiles

Copper oxide (CuO) impregnated linens are the most common anti-microbial textile deployed in health care setting though Silver Oxide (AgO), Zinc Oxide (ZnO) are also used. The combination of particle specific effects and release of metal ions by the ENM interferes with metal-ion regulated or binding proteins disrupting normal cell function and ultimately destroying the pathogen. Table 2 highlights some research on the effectiveness of ENM coated textiles in reducing HAI incidence. In some research, the efficacy of ENM costed textiles in reducing HAI incidence is explored in general while some research examines the reduction of specific pathogens on the textile surface.

Based on Table 2, we submit a HAI reduction rate of 20%, 30% and 40%. This is deemed judiciously conservative based on a survey of extant research. A complicating factor for (multiuse) nano-textiles is the wash cycle. Fabrics, textiles, and clothing used in health-care settings are disinfected and hygienically cleaned but not sterilised during laundering. Laundering cycles consist of flushing, main wash, bleaching, rinsing, and souring. Hot water washing is typically done at 75 degrees Celsius. Clean, wet textiles are then dried, pressed, folded and packaged for redistribution back to the facility.

Multiple wash cycles can reduce the antimicrobial capacity of the active metal, however, this is largely overcome by the metal silver deposition using ultrasound irradiation. In this method, nanoparticles thrown to the fabric’s surface by sonochemical microjets are high enough to cause melting and carbonization of the textile fibers. Using this method, Perelshtein et al (Perelshtein et al. 2008) showed the material staying on the fabric for at least 20 washing cycles without a reduction in the (silver) content. Given the effectiveness of the coating process and the conservative estimates of the HAI reduction rates by ENM coated materials, we feel the reduction of the efficacy of the antibacterial coating though the washing cycle can be accommodated in the existing estimates.

Costs of Antiseptics

The global antiseptics and disinfectants market size was valued at USD 16.75 billion (GrandViewResearch 2019). In 2016, the world spent USD 7.5 trillion on health, representing close to 10% of global GDP (WHO 2018). General government expenditure in the EU on health amounted to EUR 1080 billion or 7.0 % of GDP in 2017(Eurostat 2019). Using a simple ratio, this suggests the antiseptic market in the EU is valued at €3 billion per annum.

This estimate does not include the cost of application of the antiseptics which is likely to be a multiple of the purchase cost. The difficulty here lies in determining the costs of applying antiseptics. The task is performed by a large variety or healthcare personal from administrative staff (procurement), to facility distributors, cleaning staff and medical staff. For the most part, the use of antiseptics is an integral part of day-to-day patient care.

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Nevertheless, a reasonable assumption is that the application of antiseptics is double the cost of purchase at €6 billion.

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Cost of ENM Coated Textiles

The global value of the medical textile market was valued at USD 12.2 billion in 2018 and is expected to reach USD 18.5 billion by 2025 (360MarketUpdates 2019). Using the ratio of EU healthcare spend to the global spend, suggests that the EU spends € 3 billion per annum on medical textiles. The global Antimicrobial textile market is estimated to grow from USD 9.5 Billion in 2019 to USD 12.3 Billion in 2024, at a CAGR of 5.4% (ResearchAndMarkets 2019) however, these estimates include general hygiene products, not just healthcare textiles.

Using a websearch, at the time of writing, we estimate the unit cost of a high-end commercially bed sheet at €15 per meter squared. Additionally, we estimate the cost of coating this unit at € 0.30 per unit or a 2% increase in cost. The overall medical textile market includes gowns, sheets, protective wear and these products come in a variety of fabrics. However, assuming the overall EU medical textile market is valued at €3 billion, this means the additional cost of coating the textiles with antimicrobial metals is approximately €60 million (per annum).

HAI Economic Costs

HAI in Europe is responsible for approximately 16 million extra days spent in hospital per year and a quarter of all adverse events suffered by hospital patients. This amounts to an estimated direct cost of €7 billion (ECDC 2008). These costs do not include the indirect costs of lost earnings, reduced work productivity, short- and long-term morbidity and mortality or time and costs spent on hospital visits. Equally, it does not include the intangible costs of pain and suffering, or changes in life quality. In the US, Scott (2009) estimates direct costs at US $6.5 billion while Stone (2009) estimates US indirect costs between USD 28 billion to 45 billion, which entail a ratio of 4.3:1 between direct and indirect costs.

In our model, we assume a range of EU conservative direct costs only at €7, €12 and €17 billion and accordingly indirect costs of €30, €52 and €73 billion. In this study, we do not distinguish between HAI types which incur different costs. For example, pneumonia is more expensive to treat than a catheter-associated urinary tract infection. However, an aggregated total cost is sufficient to provide economic guidance.

Model Results

Based on our model, data from extant research and judicial assumptions, we find that the annual cost reduction of HAI instances in the EU by the use of antiseptics is between €557 million and €9,474 million. These numbers are in line with similar research performed by Schmier et al (Schmier et al. 2016) for US data. Using the same approach, we find that the application of ENM coated (antimicrobial) textiles is between € 304 million and € 8,038 million which is more than the antiseptic range.

More interestingly, we estimate the cost of purchasing and applying antiseptics to be about €9 billion per annum in the EU while the cost of coating hospital textiles with an antimicrobial metal is only €60 million per annum. This suggests that HAI reduction techniques and their associated cost savings should encompass ENM coated textiles as a standard tool to reduce infections.

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Nanotoxicity

This study does not incorporate the toxicity potential of NPs embedded in the functional textiles. Extant literature indicates that Copper and Silver NPs result in several adverse effects such as reactive oxygen species generation, oxidative stress, inflammation, cytotoxicity, genotoxicity and immunotoxicity(Naz, Gul, and Zia 2019; Hejazy et al. 2018; OECD 2017; Boyles et al. 2015). Physicochemical characteristics, such as particle shape, size, surface functionalization, the exposure dose, duration and mode are the main factors that define the toxicity of the nanoparticles(Furxhi et al. 2020). A paucity of exposure data through different exposure routes such as oral ingestion or inhalation route and data lacunas regarding the key physicochemical properties that influence the toxicity of NPs, makes the integration of toxicity out of the scope of this study. A case-by-case hazard assessment of the nanomaterials is needed in each case to incorporate the toxicity into the economic evaluation. While a comprehensive understanding of the risks to patients and staff is some way off, the economic costs of those risks is difficult to gauge at the time of writing. One practical pathway would be to measure the increased costs, if any, to insurance premiums.

Conclusion

Health care-associated infections (HAIs) are a considerable economic burden to the global health sector directly costing USD 6.5 billion and additional USD 28 billion to 45 billion of indirect costs, in the US alone. These amounts ignore the societal costs and the incalculable suffering caused to victims of HAIs. In Europe, 7% of all admissions to acute hospitals result in a HAI with 37,000 direct fatalities and up to 110,000 fatalities if indirect deaths are included.

The current approach to combatting HAIs is pragmatic and focused on staff training, patient identification and isolation, use of antiseptics, antibiotic prescription monitoring and so on. Despite these measures, a flawed implementation and the nature of the pathogen suggests that the effectiveness of current methodologies may have plateaued.

ENMs have been considered to be the ‘‘material of the 21st century”. There is a significant body of research to show that surfaces ameliorated with ENM, particularly copper and silver oxides, can reduce the biological burden and therefore reduce the incidence of HAIs in health care facilities. The active agent of the coating is constant and perpetual. Textiles are a discrete surface type that are amenable to microbial persistence because of the nature of the material, the moisture and temperature conditions present and the very large surface area. These provide an ideal environment for microbial proliferation.

Our research shows that approximately similar amounts of money are spent on antiseptic and on hospital textiles per annum, namely €3 billion. In examining the relative effectiveness of ENM coated textiles against antiseptics, we find that coating textiles with antibacterial ENMs is potential more effective than antiseptics. Furthermore, the additional cost of coating textiles with an ENM antibacterial substance is relatively inexpensive. In addition, coating textiles with an ENM does not require expansive monitoring. One potential impediment to the large scale roll-out of ENM coated textiles is the absence of a clear understanding of the human and environment risks posed by nanoparticles. These risks will negatively impact both the clinical and economic benefits afforded by ENM coated materials but it is not possible at this time to measure that impact.

To be clear, this is not an *either-or* situation. We use the effectiveness of antiseptics only as a means to judge the relative effectiveness of ENM coated textiles. We also acknowledge the relative paucity of information, the heterogeneous nature of the data and the suppositions (though conservative ones) made in our analysis. While our approach is not a rigorous economic analysis due to the lack of data, it is, nonetheless an important first step in determining the efficacy of ENM coated materials. Accordingly, our results and suggest a greater investment in ENM coated textiles is economically justified and certainly warrants further, detailed and comprehensive analysis. A note of caution is warranted given the current lack of knowledge regarding the safety in use of ENMs used in textile industry. If scientific evidence was sufficiently robust, regulators may mandate the use of ENM coated textile. Yet the current lack of knowledge suggests that some regulatory measures should be taken. These measure in turn, may increase the cost of these ENMs and thus question their cost effectiveness.

In this paper we have outlined the effectiveness of ENM coated textiles in reducing the incidence of HAIs. Despite this, there is a notable absence of wide scale usage of this technology in clinical settings. This is due, in part, to regulatory hurdles, human and environmental risk uncertainty and a paucity of clinical evidence. In our view, it will be necessary to provide a systematic test approach involving academic, clinical and commercial interests. The success, or otherwise, of these tests will ultimately be determined by the economic viability of the approach and, while we have determined that this is likely to be cost effective, the economic modelling needs to be included as part of future systematic testing.

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5. Generalized Use Case

Generalizing the HAI Use-Case

HAI In-depth Analysis

The use-case setting and economic evaluation presented in section 4 show that there is a significant potential economic advantage to using ENM costed textiles in a health care setting. Aside from the economic advantage, the reduction in hospital days and illness associated with HAIs would be a significant social benefit. The approach used, is not without its drawbacks and we list three main criticisms here. First, the approach used whereby the economic efficacy of ENM coated textiles is compared against traditional antiseptics suggests independence between the two reduction techniques which is not realistic. The second criticism is the extrapolation of data and the assumption of homogeneity both across the EU and across the health sector. Third, the approach used does not include the economic risk of ENMs in the health care sector or in the manufacture, washing and disposal of the textiles.

These shortcomings are entirely valid but, whatever the use case, they are likely to be present. In this sense, section 4 is an important foundation in that it highlights the likely economic impact of ENMs and throws up many of the challenges in developing economic guidelines in a general sense. This section then meets those challenges and proposes a more robust economic approach to the use case selected.

The question posed is; how effective would the introduction of ENM coated hospital textiles be in reducing the incidence of HAIs. Once that has been devised, hospital managers and national health authorities can determine the economic effectiveness of introducing those textiles on a large scale basis.

The economic approach is to gather data for as many hospitals as possible. The dependent variable is the incidence of HAI in the hospital and the independent variables “explain” the incidence of HAI in that hospital. The independent variables include the doctor/patient ratio, the number of beds and intensive care beds, the university hospital designation and so on. Crucial to the approach is the gathering of as much relevant independent variables as possible. Once the data has been gathered, then in theory, all incidences of HAI can be “explained”, however, in practice this is not the case and the unexplained variance can be ascribed to the excess presence of pathogens in the hospital surfaces.

This section describes the methodological approach. The actual gathering of data and data analysis is being carried out but, at the time of writing, the results and analysis are not available. Note that, although of interest, the results are less important than a description of the methodology employed in the context of developing guidelines for economic assessment of ENMs

First, we recognise that HAI incidence is associated with different pathogens in different contexts. Invasive procedures are most likely to result in a HAI. For example, in the EU 2017, 8.3% (11 787) of the patients who stayed in intensive-care units (ICUs) for more than two days presented with at least one ICU-acquired healthcare-associated infection (HAI) under surveillance (pneumonia, bloodstream infection, or urinary tract infection)(ECDPC 2019).

The three most common types of HAIs are related to invasive devices or surgical procedures and include

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1. Catheter-associated urinary tract infection (CAUTI)

   An infection involving any part of the urinary system, including urethra, bladder, ureters, and kidney. UTIs are the most common type of healthcare-associated infection reported to the National Healthcare Safety Network (NHSN). Among UTIs acquired in the hospital, approximately 75% are associated with a urinary catheter, which is a tube inserted into the bladder through the urethra to drain urine. Between 15-25% of hospitalized patients receive urinary catheters during their hospital stay.(CDC 2019)

2. Central line-associated bloodstream infection (CLABSI)

   A central line (also known as a central venous catheter) is a catheter (tube) that doctors often place in a large vein in the neck, chest, or groin to give medication or fluids or to collect blood for medical tests. Central lines are different from IVs because central lines access a major vein that is close to the heart and can remain in place for weeks or months and can be much more likely to cause serious infection. Central lines are commonly used in intensive care units.

3. Surgical site infection (SSI)

   A surgical site infection is an infection that occurs after surgery in the part of the body where the surgery took place. Surgical site infections can sometimes be superficial infections involving the skin only. Other surgical site infections are more serious and can involve tissues under the skin, organs, or implanted material.

Two of the most common microbial pathogens involved in HAI incidences are;

4. Methicillin-Resistant Staphylococcus Aureus (MRSA)

   A MRSA infection is caused by a type of staph bacteria that's become resistant to many of the antibiotics used to treat ordinary staph infections. Staph skin infections, including MRSA, generally start as swollen, painful red bumps.

5. Clostridium difficile (C.diff.) Infection (CDI)

   Clostridium difficile, also known as C. difficile or C. diff, is bacteria that can infect the bowel and cause diarrhoea. The infection most commonly affects people who have recently been treated with antibiotics. It can spread easily to others.

We use these five HAI associated variables as dependent variables and test how they are ‘influenced’ a series of independent variables. The more independent variables the more likely they can fully ‘explain’ the dependent variables and therefore explain the incidence of HAI. When all HAI events are almost all explained, the unexplained variations (events) can be ascribed to HAI from bed linen, hospital gowns, pyjamas and from hard surfaces such as flat screens.

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Figure 8 - Sources of pathogens in an acute hospital room. Source:wikipedia(Wikipedia 2020)

The independent variables in our ongoing research will contain 20 control vars. including, but not limited to:

1. Type of hospital by: Private, public,
2. Is it a university hospital?
3. Type of hospital: General, Geriatric, Rehabilitation, Children, Mental, etc.
4. Establishment year
5. What surgical departments exist? Trauma, orthopedics, obstetrics, gynecology, oncology, hematology, pedriatrics, etc?
6. Is there a core unit in burns, what is the annual number of patients?
7. Number of general beds and number of intensive care beds.
8. Number of patients admitted for a period.
9. Volume of Medical Personnel in Intensive Care Departments (Physicians and Nurses)
10. Average number of beds in inpatient room

And more. At the time of writing, this research is ongoing and will continue past the delivery date. The results of that research are less important than the methodology which we will describe here.

Methodology

Panel (data) analysis is a statistical method, widely used in social science, epidemiology, and econometrics to analyze two-dimensional (typically cross sectional and longitudinal) panel data(Maddala and Lahiri 1992). The data are usually collected over time and over the same individuals and then a regression is run over these two dimensions. Multidimensional

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analysis is an econometric method in which data are collected over more than two dimensions (typically, time, individuals, and some third dimension).

A simple panel data regression model has the form

$$y_{it} = a + bx_{it} + \varepsilon_{it}$$

where *y* is the dependent variable, *x* is the independent variable, *a* and *b* are coefficients, *i* and *t* are indices for individuals and time. The error term ε_{it} is very important in this analysis because assumptions about the error term determine whether we speak of fixed effects or random effects. In a fixed effects model, ε_{it} is assumed to vary non-stochastically over i or t making the fixed effects model analogous to a dummy variable model in one dimension. In a random effects model, ε_{it} is assumed to vary stochastically over i or t requiring special treatment of the error variance matrix.

We suppose that the independent variables do not vary across time and therefore we will conduct a fixed effects panel test. To test whether fixed effects, rather than random effects, is needed, the (Durbin-Wu-) Hausman test can be used.

Obs	**i**	**t**	**HAI Rate (%)**	**Hosp. type**	**No. ICU Beds**	**Ratio Patients to Doctors**	**etc**
1	1	2010	8.8	Public	16	8.7	
2	1	2011	8.7	Public	16	8.8	
3	1	2012	8.9	Public	16	8.6	
4	1	2013	8.5	Public	18	8.6	
5	1	2014	8.5	Public	18	8.5	
6	2	2010	7.3	Private	10	6.9	
7	2	2011	7.5	Private	10	6.9	
8	2	2012	7.6	Private	10	6.8	
9	2	2013	7.5	Private	10	6.7	
10	2	2014	7.7	Private	10	6.7	
11	3	2010	9.1	Public	22	9.1	

Table 3 - Example of panel data (also known as longitudinal data)

Table 3 provides an example of a panel data set because we observe each hospital *i* in the data set at five points in time (the year 2010 to 2014 inclusive). At the time of writing we are gathering information on several EU and US hospitals. With panel data, we reference observations by *t* as well as i to distinguish between our observations of a hospital *i* at various points in time:

$$HAI_{it} = \beta_0 + \beta_1 HT_{it} + \beta_2 IB_{it} + \beta_3 PDR_{it} + \alpha_i + \delta_i + \varepsilon_{it}$$

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where the *i* represents the hospital fixed effects and the *t* represents year fixed effects. *i* can be thought of as shorthand for a set of dummy (indicator/binary) hospital variables each multiplied by their respective regression coefficients (that is, a dummy variable for each hospital multiplied by its regression coefficient. Similarly, it can be thought of as shorthand for a set of dummy year variables each multiplied by their respective regression coefficients (that is, a dummy variable for each year multiplied by its regression coefficient.

δ_t estimates the common change/difference (to all hospitals) in the HAI rate in year t relative to the year 2010, controlling for Hospital Type, No. of ICU Beds and Patient to Doctor Ratio hospital-specific time-invariant characteristics (the hospital fixed effects). We call δ_t a year fixed effect because the change is common to all hospitals in year t; in other words, the `effect' of year t is ‘fixed' across all hospitals.

Similarly, α_t estimates the common change/difference (to all years) in the HAI rate in hospital i relative to hospital 1, controlling for Hospital Type, No. of ICU Beds and Patient to Doctor Ratio common to all hospitals (the year fixed effects). We call α_t a hospital fixed effect precisely because the difference is common to all years in hospital i; in other words, the `effect' of hospital i is `fixed' across all years.

β_1 is the estimated effect of Hospital Type on HAI, controlling for hospital-specific time-invariant characteristics and year-specific shocks (the hospital and year fixed effects). β_2 and β_3 have similar explanations.

After the full data set has been collated, the distributions of the variables can be estimated. With a probability distribution, we can generate more data by simulating data by randomly sampling from the distribution. This random sampling of data from distributions is known as a Monte Carlo simulation and effectively allows us to exponentially increase the sample size.

In our continuing research, when our data has been gathered, we will run five models of fixed effect regressions, three for each of the specific HAI occurrence and two for the two pathogen types. By initially creating five models, this will allow us to understand the differences and their significance in an overall HAI effect approach.

The unexplained variation of these regressions can be viewed as the (upper limit) of the effect of medical textile on the incidence of HAI. Assuming success, it is somewhat trivial to determine the economic cost of a) an absence of ENM coated textiles and b) the introduction of ENM coated textiles. The latter would include their cost to purchase, any additional washing costs (if any) and their reduction of HAI incidence. The cost of the HAI incidence is generally available for a specific region.

General Methodology

The fixed effects panel data approach is an appropriate methodological approach in most instances. To demonstrate this, in this section, we discuss an application of the above methodology in a more generic case not related to the previous analyses on application of ENMs as antimicrobial agent in hospital textiles.

Water pollution by various toxic contaminants has become one of the most serious problems worldwide, particularly in developing countries. Various technologies have been used to treat water and waste water including chemical precipitation, ion-exchange, adsorption, membrane filtration, coagulation–flocculation, flotation and electrochemical methods. In the past few decades, nanotechnology has gained widespread attention and various nanomaterials have been developed for the water remediation (Santhosh et al. 2016).

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Carbon nanomaterials, nano metal oxides and nano composites have been used for water decontamination.

Beyond water treatment, intelligent environmental nanomaterials have been proposed and are at the early stages of development. This could be deployed in filtration membranes with responsive gates, materials with on-demand oil/water separation, environmental materials with self-healing capability, and emerging nanofibrous air filters for PM2.5 removal (Chang, Zhang, and Wang 2018).

Looking specifically at water desalinisation as an economic problem, we first note the increasing demands on global freshwater resources and the concurrent increasing evidence of climate change. These twin forces are particularly problematic for developing countries. Desalinization of salt water is one potential solution and one that can be achieved through a solar distillation system with nanofluids for increased efficiency (Rashidi et al. 2019). Other methods using nanomaterials are available.

In an economic modelling context, we need to define first what we are measuring as a dependent variable. This could be a micro variable such as the aggregate cost of fresh water provision to a region. It could also be the mean household water bills. This approach misses a broader (welfare economic) perspective that includes other societal benefits. These include but are not limited to societal health outcomes (infant mortality, sickness rates, life expectancy rates), food security outcomes (security of water supply equates to security of food supply) and other societal benefits.

The dependent variable (what we want to measure) can be one or more of these variables. In the case where the cost of fresh water is the dependent variable then the independent variables can be the investment in infrastructure (that includes the nano component), the cost of power and/or the investment in solar technology.

The use of Societal Health Outcomes as a dependent variable is obviously more complex but certainly possible. If the dependent variable is chosen to be “life expectancy”, “infant mortality”, “educational level” etc then the availability of a constant food supply, educational access, healthcare access, and GDP can be independent variables along with a range of other societal factors. In a fixed effects panel regression, with sufficient and relevant explanatory variables, the unexplained variance can be assigned to the availability of fresh water. The data should be gathered over a number of years for a longitudinal analysis. The cost of that availability can then be determined and a cost-benefit analysis devised.

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6. Guidance on assessment of economic benefits of ENMs

In the previous Chapters, different methodological approaches are described and exemplified through the use of example cases. Establishing WTP through a choice based conjoint analysis was presented in Chapter 2. In Chapter 4, aggregate annual cost reductions are estimated using relative cost-benefit analysis, and Chapter 5 outlines a univariate procedure using panel data to attribute unexplained variation to the effect of medical textiles on HAI incidence as well as a more generalized version as a starting point for CBA and eventual welfare economics assessment. All approaches have their advantages and disadvantages.

WTP is a very effective approach, particularly for gauging market demand for a nano-enabled product. Furthermore, this approach can capture the risk sensitivities of the customer, be that individuals or corporate customers. In order to effect this analysis, an appropriate and detailed survey must be completed by a significant subset of the customer base. This is normally done by a questionnaire. This difficulty of this approach, for the purposes of forming an economic guideline, is that the survey of customers should be completed with a specific product in mind. That is, it is not reasonable to ask the respondent generic questions on abstract products and derive a WTP approach. For example, a WTP approach can be used to decide if a customer would prefer a nano-enhanced lipstick or a nano-enabled water filtering system but the WTP results will be specific to those two use cases and difficult to extrapolate to a general approach.

The Welfare Economics approach can take a macro approach to determine the overall economic benefit of nanomaterials. We cite a useful analogy with a welfare economics approach to climate change with a specific Cost Benefit Analysis approach. The list of challenges of an analysis of climate change on the economy and an attendant economic analysis is long. The risk uncertainty across generational groups and non-market valuation in climate change analysis is mirrored in the challenges facing an economic analysis of the benefits and risks of nanomaterials.

That said, for decision making a CBA based on welfare economics can provide useful information by deploying existing state-of-the-art tools and methods. Clearly an improvement of the underlying methodology and, more importantly, improving an understanding of the risk of nanomaterials to humans and the environment is critical. Should these aspects of a CBA be improved as well as expanding the CBA to explore additional dimensions of decision making would further increase the ability of Welfare Economics to assist decision makers. Incorporating Multi-criteria analysis (MCA) and Robust Decision Making (RDM) tools into an CBA/Welfare Economics approach would also stimulate dialogue with stakeholders.

To aid in determining the type of economic assessment, the different approaches outlined in this document are presented in the shape of a decision tree, presented in Figure 9. Note that this decision tree is indicative only.

CBC and WTP are approaches most suited for ENM producers, i.e. they give an estimate of market potential for an ENM product or product group. Combined with a micro-economic production function, establishing (marginal) costs of production, a producer may quantify revenue as well as costs. Assuming the producer intends to maximise profit, by pursuing a strategy where its marginal costs equal marginal revenue, and has market power without price differentiation (i.e. is a homogenous price setter), a consumer and producer surplus may be estimated, as well as any welfare (deadweight) loss associated with the price

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differing from its free market equilibrium. Production functions may be modelled using a simple Cobb-Douglas or Leontief type model.

For (industrial) consumers of ENM products or product groups a relative CBA is recommended, which estimates the costs or benefits of utilising ENMs by weighing potentially avoided adverse effects by application of ENMS against the economic costs of ENMs. This approach relies heavily on assumptions and estimations of macro-economic parameters such as total market size, but can give a quick overview of direct and eventual indirect benefits of application of ENMs. The latter though, may be hard to quantify for reasons outlined in Chapter 2, such as ubiquity of impacts and intangibility.

It should be noted here that the production or consumption scope does not preclude the application of WTP or CBA, but rather the suitability of each approach for each perspective. In addition, direct and indirect negative effects of production or utilisation of ENMs are not explicitly included, though to an extent they are factors in WTP (through actual or perceived risk) as well as through additional costs in the CBA. Economic assessment should therefore be complemented with other risk and benefits assessments covering topics such as human and ecotoxicology, environmental impacts and ethical and societal perspectives.

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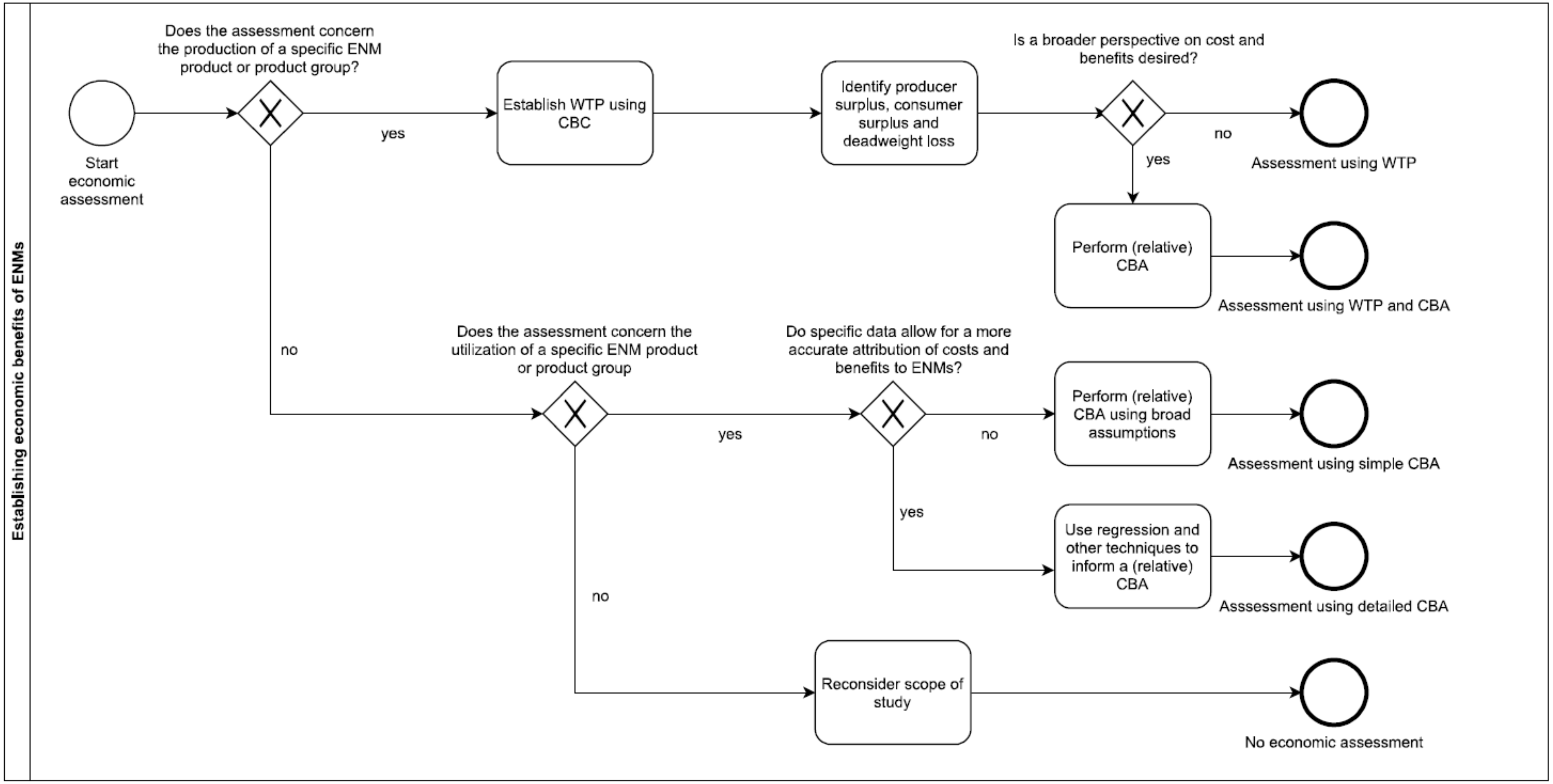

Figure 9: Decision tree to aid in determining the economic benefits associated with production or use of ENMs.

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7. Risk Adjustment

ENM Economic Impact

The absence of clear ENM risk assessment is a significant limiting factor in the economic approaches described. That is, to this point, we have assumed that the ENM enabled products are benign and do not pose a risk to human or environmental health. Of course, there are risks in the manufacture, application and disposal of ENMs and these risks come with concurrent economic costs.

The International Organization for Standardization (ISO) standard 31000 defines risk as the "*negative or positive deviation from what is expected due to uncertainty on objectives,*" linking risks to uncertainties. To reduce uncertainties and risks, it is thus necessary to gather reliable, balanced, and objective data and information to form a risk-benefit analysis. Communication of risk and uncertainty related to decision making is a crucial component of health risk communication to ensure the appropriate use of risk information and to enhance the understanding of uncertainty among the users of risk information, such as risk managers (that is, decision makers), journalists, non-governmental organizations (NGOs), citizens and other relevant stakeholders. However, a transparent process and framework for science-informed RG is currently absent.

In the absence of a clear risk assessment approach, economic guidelines will not be effective. Within RiskGONE, D3.1 Draft guidelines for risk assessment and D3.7 Draft guidelines regarding bringing together risk indicators can be used as input parameters for future iterations of the economic guidelines. It is important to distinguish between real and perceived risk, both of which can impact the economic guidelines. For real risk, an alternative approach of to use risk transfer pricing as a metric by examining the direct cost of the risk as determined by an insurance policy.

8. Conclusions

In this report, we detail three approaches to produce economic guidelines or economic methodologies. First, we examine a Welfare Economics approach. Welfare economics is defined as a branch of economics that studies how the distribution of income, resources and goods affects the quality of living standards in an economy. Creating economic guidelines for nanomaterials using a Welfare Economic approach is analogous to creating economic guidelines for climate change. Therefore, the welfare economics approach is certainly challenging but not unattainable in the long term.

Economic welfare can be measured using a range of variables such as GDP and other indicators that reflect the welfare of a population (such as literacy, number of doctors, levels of pollution etc). Economic welfare is concerned with more than just levels of income such as an economy's GDP. Important to people's living standards are actors such as levels of health care, and environmental factors, such as congestion and pollution. These quality of life factors are important in determining economic welfare.

The problem of applying an economic model to Engineered Nanomaterial usage is the scale and range of their current and future usage. We see both the range of nanomaterials, their characteristics and potential toxicity as one challenge. On the other hand, the range of current and future applications of nanomaterials is significant. These large scale domain parameters are effectively multiplied to create a significant challenge in determining the utility and socio-economic benefits. This can be made more manageable if a subset of nanomaterials that pose societal risk are identified. The balance of nanomaterials and their usage can then be regarded as being of a net positive effect.

Willingness to Pay (WTP) is a very useful economic and marketing tool and of particular benefit when determining the economic advantage of a product or range of products. Willingness to pay (WTP) is the maximum amount an individual or company is willing to pay to obtain a product or service. If the consumer is indifferent to buying or not buying, then that price reflects the product's inherent value in monetary terms. That is, the product and the money have the same value, so spending to obtain a product is the same as keeping the money.

WTP has another advantage in that it can incorporate a consumer's WTP an additional price for a product with an additional utility afforded by a nanomaterial. Additionally, if the risks of the nanomaterial are also described then the consumer can adjust the price point to incorporate their perceived risk.

There are multiple design approaches to a WTP model. The most popular is a Conjoint analysis with this approach permitting a realistic evaluation of choices among hypothetical features that vary simultaneously: conjoint = "consider jointly". Conjoint analysis is a popular method of product and pricing research that helps uncover preferences for product features, sensitivity to price, forecast market shares, and predict adoption of new products.

We find that a WTP approach is an excellent approach to a particular product or range of products but the methodology is product specific. That is, a consumer survey or questionnaire concerning a particular product cannot be representative of a heterogeneous product group that would allow for a broader economic interpretation. That said, as with the welfare economics approach, if a subset of nanomaterials of particular interest (risk) were identified then a series of WTP would provide a snapshot of perceived risk versus beneficial utility.

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In our research, we selected a case study to understand the complexities of one usage of ENMs and then extrapolate from there to a broader socio-economic case. The ENM coated hospital textile case study was selected for several reasons. First, ENMs have significant potential as an anti-microbial active ingredient and recent scientific and technical advancements allow for the embedding of the ENM in the textile. Second, Healthcare Acquired Infections (HAIs) can be reduced through the use of antiseptics and a rigorous hand washing regime but HAI rates persist in the 5-10% range in developed economies causing significant additional fatalities and adverse health outcomes. This results in billions of Euros lost in additional healthcare costs and societal losses. Third, the use of ENM coated textiles comes with the attendant questions regarding the potential toxicity of the ENM. This toxicity can manifest itself in the production process, in the use of the textiles in a hospital setting and the washing and eventual disposal of the textiles.

We started out research by examining the problem domain and then devised a strategy to compare the potential economic effectiveness of ENM coated textiles against a traditional antiseptic approach. To be clear, we compare the economic efficacy, not a clinical either-or scenario. We found significant evidence that, certainly, ENM coated textiles should be tested in a more rigorous and comprehensive setting. Our findings were published in a peer reviewed journal (Murphy, Tchetchik, and Furxhi 2020).

From this platform, we developed an examination of the case-study further by gathering data on a number of US and EU hospitals over time. This research is continuing and will use a fixed regression panel data to effectively explain the incidence of HAI occurrence in hospitals with any unexplained residual variance being attributable to the existence of pathogens in hospital textiles. This rigorous econometric approach will then allow us to more effectively describe the economic case for the widespread use of ENM coated textiles in healthcare settings.

This precise approach to examining one particular case study on the use of ENMs is particularly effective in showing the difficulty of deriving general socio economic guidelines but we have also shown that a methodological approach is entirely possible. Welfare Economics can be seen as the ultimate goal where the economic benefits along with the societal benefits can be measured. This maybe some time off but in the long term is quite attainable. Willingness-to-Pay is an effective methodology for a product or product group analysis. It can also factor in customer perceptions of risk. This analysis then could be used by regulators to gauge how a regulatory approach would be reflected in consumer price sensitivity.

The case-study and extrapolation approach used in our research shows that a fixed regression panel test is an effective utility methodology that can be used in most circumstances.

One deficit of our methodological guidelines is the general absence of the inclusion of risk. For example in our ENM hospital textile case study, we showed the economic effectiveness of using ENM coated materials in a clinical setting. We did not, however, factor in the human and environmental risk in the manufacture, usage and disposal of these materials. This is largely due to the lack of a clear consensus on risks posed by the material. This is understandable as the exact characteristics of the ENMs should be known, the manufacturing process should be studied and the likelihood of the ENM dispersing and exposure setting during the manufacture, usage, washing and disposal. The risk to human and environmental health remains a difficult scientific question and until that is clarified,

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estimating the attendant economic risk will remain a challenge. That said, one approach is the estimation of the additional cost of risk as measured by the insurance premium offered by insurers to manufacturers and users of ENMs. This will be covered in the next phase of T3.3 when the role of underwriting will be examined in more detail.

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