

Modelling Pathways for Outbreaks in Field Occupational Epidemiology

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Abstract

Background: The investigation of an occupational outbreak, once the index case has been identified, triggers a stress situation to epidemiologists. Modelling occupational outbreaks will be useful to guide the field investigation. **Objective:** To identify standard pathways for occupational epidemic outbreaks. **Methods:** In-depth critical appraisal of 57 occupational outbreaks. Standard pathways of occupational outbreaks were identified by analysing the similarity between out-breaks. The model's accuracy and homogeneity were established through Fisher's exact test and the Kappa Index. **Results:** The analysis allowed synthesizing the occupational outbreaks variability in 4 pathways. 92.98% of the analysed outbreaks could be allocated to one of those 4 types. The theoretical patterns showed a good adjustment with the analysed out-breaks: Type I (Kappa = 0.94 - 0.60), Type II (Kappa = 1.00), Type III (Kappa = 1.00 - 0.68) and Type IV (Kappa = 0.94 - 0.87). The probability of a given outbreak fitting with its three components in any of the theoretical pathways was 0.83. **Conclusions:** The incorporation of those pathways to the field occupational epidemiology will allow: 1) to provide early guidance to epidemiological, clinical and environmental studies focused on specific hypothesis of causality; 2) to anticipate preventive measures; 3) to contribute to an earlier and more efficient outbreak resolution.

Keywords

Occupational Outbreak, Occupational Diseases, Working Exposure, Field Epidemiology

1. Introduction

Working environment as part of the disease aetiological complex was already

evidenced by the empirical observations of Bernardino Ramazzini (1633-1714) reported in “De Morbis Artificum Diatriba” [1].

Ramazzini’s contribution to the medical reasoning was to include the study of the occupational activity and work-related exposure in the disease interpretation and the explanation of its causal complex.

The workplace environment is included at the core of the public health concept as a determinant of collective health. In this sense, health and wellbeing related to specific working conditions are incorporated into the morbidity profile of different territories and population groups.

Marisa Corfiati *et al.* [2], evidence how the location of mesothelioma clusters in the Italian municipalities is associated with the economic development of the asbestos industry in those territories.

The main epidemiological intelligence agencies: Europe-CDC [3], USA-CDC [4], Australia NHNRC [5] systematise the outbreak investigation in a series of steps, which includes, these components: Person, time and place and the corroboration of causal hypotheses by statistical methods. In spite of accepting this system, difficulties are found for its application in the field of occupational epidemiology. Jorma Rantanen [6] at the International Conference “New Epidemics in Occupational Health”, held in Helsinki in 1994, warns about the difficulties in identifying occupational clusters and applies the term “silent epidemics” when referring to them.

Schulte *et al.* [7] add the difficulty of applying statistical methods in the study of occupational clusters. After analysing 61 clusters of occupational cancer investigated by the US National Institute of Occupational Safety and Health (NIOSH), Schulte proposes that to investigate occupational cancer clusters less “quantitative epidemiology” and more “interpretative epidemiology” is needed.

Just like Ramazzini proposed to add to the three Hippocratic questions a new one: “What is your occupation?” [8], it is necessary to add to the three conventional components in field epidemiology a new one, a “technological component”: Person-Time-Place-Technology.

The importance of studying this technological component in occupational epidemiology is demonstrated by Moya *et al.* [9] when investigating an outbreak of 22 cases of organising pneumonia. The analysis of the “technological component” allowed us to conclude that all cases were workers of the textile industry, 20 cases from only 2 companies (RR = 24.3; 95% CI = 5.7 - 104.4) and all of them were involved in textile printing by spraying procedures.

The work process mapping and its analysis have a special interest for field occupational epidemiology since it allows identifying the risk exposure at the exact point where it occurs and whether it affects one or several tasks and, therefore, one or several workers’ groups.

The importance of overlapping the “technological component” with “time” and “place” is evidenced in the outbreak reported by Zimmermann *et al.* [10].

In that outbreak, Zimmermann analyses the “technological component” by mapping the cases through the working process, which we can call a “technolo-

gical map of cases”, showing that its occurrence was sequential across the working process, and showed a concordance in time with the path of the raw material.

Therefore, considering that working processes can be standardised and that cases have a limited distribution at the plant, we can formulate the hypothesis that occupational out-breaks follow some patterns. This would allow to synthesise its variability in a limited number of Standard Occupational Outbreak Pathways and to formulate the main objective of characterizing them according to the following components: Technological linkage, place at plant, and potential causal agent.

The matter concerning the model’s adequacy may be analysed by means of the following specific goals: 1) to identify the fit between theoretical models and real outbreaks; 2) to check the internal homogeneity of each pathway; and 3) to identify the prevalence and the probability of the different epidemiological pathways.

2. Material and Methods

In-depth critical appraisal of occupational outbreaks, published between January 2000 and May 2014, in journals indexed in PubMed. The collection to be studied was recovered by means of an advanced search builder including the following terms: Outbreak OR epidemic AND occupational asthma/Outbreak OR epidemic AND occupational dermatitis/Outbreak OR epidemic AND occupational cancer/Outbreak OR epidemic AND occupational exposure.

Articles that met all the inclusion criteria were included for analysis, and articles that met at least one of the exclusion criteria were excluded (**Table 1**).

In order to identify the specific characteristics of occupational outbreaks and to establish the elements to summarise their variability, a sample of the total collection was analysed. The sample was selected systematically according to the order of the full text review, and the sampling quota was higher than 50% of the

Table 1. Eligibility criteria.

Inclusion criteria	<ul style="list-style-type: none"> • Original papers • English or Spanish language • Published between January 2000 and May 2014 • Sick population were workers • Outbreaks started in a working environment
Exclusion criteria	<ul style="list-style-type: none"> • Occupational outbreaks arising in the context of major pandemics (e.g., severe acute respiratory syndrome, avian influenza) in order to avoid that an excess of publications in this health alerts could modify the profile of outbreaks in working environments. • Public health or environmental outbreaks (mediated by vectors, water, foods, etc.) as they are far from the subject of the study due to their epidemiological characteristics. • Outbreaks of person/person transmission, since their occupational origin may be uncertain. • Outbreaks of zoonosis by contact with live animals not arising from professional activities: wild or domestic animals, etc.

total collection.

In order to extract information, a synthesis matrix was designed and relevant epidemiological and scientific information was collected.

The similarities between outbreaks were analysed for the following epidemiological parameters: 1) Links between cases and working process; 2) Spatial distribution of cases; 3) Agents or risk exposure potentially involved.

The standard pathways of occupational outbreak (SPOO) were formulated based on the similarities of those three epidemiological parameters.

The internal homogeneity of each defined SPOO was analysed with Fisher's exact test.

The fit between components (technological linkage, spatial distribution and agent involved) for each SPOO was analysed by the Kappa index.

The probability analysis for the occurrence of each SPOO was carried out by analysing the combined probabilities of the three components taken one by one, on the basis of one sequence: Spatial distribution -> Technological relationship -> Agent involved.

The variability of presentation typologies was calculated through the number of variations with replacement of four elements (types of behaviour), taken in three-by-three elements (analysed components).

3. Results

The results obtained in the search process are shown in (Figure 1). A total of 57

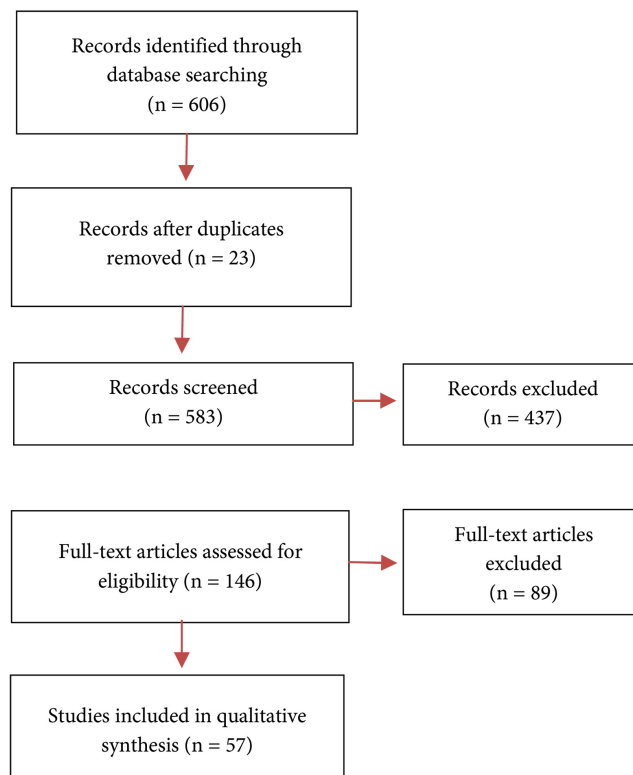


Figure 1. References reviewed and selected for study.

articles were recovered, and a sample of 33 articles was selected to be analysed in the process of characterisation of the standard pathways of occupational outbreak.

Out of the 33 outbreaks analysed (**Table 2**), 13 reported that the outbreak occurred among workers performing a specific task of the production process [11]-[23]. No cases were reported of workers involved in other activities, except additional cases that occurred nearby as a result of an environmental spread of the contaminant [14] [17] [18].

In this group of 13 outbreaks, there was not always information concerning all the aspects related to occupational exposure, preventive measures or working conditions, but in these outbreaks there was a concurrence of causes regarding: the exposure to conventional substances or products handled while performing a specific task [14] [16] [17] [18] [19] [21] [22] [23], innovation processes [11] [12] [13] [15], poor working conditions [11] [12] [13] [17] [18] [21] [22] [23], unusual operations within the working process [14], improperly performed processes [15] [18] or ancillary contaminated products [19].

Out of these 13 outbreaks, 6 reported on the spatial distribution of cases. All of them showed that the outbreak was limited to the plant area where the task related to exposure to the causal agent took place [16] [17] [18] [20] [21] [23].

In other 8 outbreaks (**Table 3**), out of the 33 analysed, the cluster occurred among workers who performed different tasks within the working process but technologically linked by a common exposure to products or substances with a cross-sectional use [24]-[31]. Cases were limited to these tasks-areas, except additional cases nearby as a result of an environmental spread of contaminants [24] [25] [28] [30].

The causal agents described in the analysis were related to substances or ancillary products used to operate machinery [24] [25] [27] [31], personal protective equipment or work clothes [26] [29], innovative processes [27] or poor working conditions [28].

Out of these 8 outbreaks, 6 reported the spatial distribution of cases, which involved several plant areas where different tasks were performed, but shared the exposure to the causal agent [24] [26] [27] [28] [30] [31].

In 8 of the 33 analysed outbreaks (**Table 4**), the cluster occurred with workers involved in different tasks within the working process in a sequenced way. Cases were linked to the route of the contaminant through the production stages [32]-[39], with additional cases reported nearby as a result of an environmental spread of the contaminant [33] [37].

In 5 of these 8 outbreaks, authors reported the spatial distribution of cases [33] [34] [35] [36] [38], showing a distribution involving several areas of the plant where consecutive tasks of the working process were performed.

The causal agents described are related to: innovative processes [32], raw material additives 36, raw material deterioration [33] [34] [35] [39], concurring or not with poor working conditions [37].

Table 2. Synthesis of outbreak information regarding to occupational relationships (I).

Information regarding to occupational relationships (I)							
Ref.	Title	Task performed (relationship between cases)	Agent/risk exposure	Environmental spread	Exposure circumstances	Concurrent facts	Cases location
11	Contact dermatitis from methylisothiazolinone in a paint factory	Pouring additives into a mixing container in the production of water-based paints	Methylisothiazolinone	-	Innovation Processes (new preservative)	Poor working conditions	-
12	An epidemic of occupational contact dermatitis from an acrylic glue	Examine coils for defects and manual disassemble the defective ones	Acrylic glue	-	Innovation Processes (new glue)	Poor working conditions	-
13	Concomitant contact allergy to the resins, reactive diluents and hardener of a bisphenol A/F-based epoxy resin in subway construction workers	Insertion of iron bars into concrete walls in the construction of new subway stations	Bisphenol A/F-based epoxy resin system	-	Innovation Processes (new resin)	Poor working conditions	-
14	Allergic contact dermatitis from dicyclohexylmethane-4,4'-diisocyanate	Cleaning a centrifuge after a massive contamination of DMDI	Isocyanate dicyclohexylmethane-4,4'-diisocyanate (DMDI),	Additional cases due to an environmental spread of the agent	Conventional products in the task performance	Non-routine operations	-
15	Occupational allergic contact dermatitis in a company manufacturing boards coated with isocyanate lacquer	Operators by the machine lacquer	Ddiphenylmethane-4,4'-diisocyanate (MDI)	-	Innovation Processes (new lacquer)	Processes developed improperly	-
16	New-onset asthma associated with exposure to 3-amino-5-mercapto-1,2,4-triazole	Charge AMT into production vessel	3-amino-5-mercapto-1,2,4-triazole (AMT)	Environmental spread. No additional cases	Conventional products in task performance	-	Task siting place
17	Epidemiologic investigation of immune-mediated polyradiculoneuropathy among abattoir workers exposed to porcine brain.	Removing porcine brains with compressed air	Aerosol nervous tissue	Additional cases due to an environmental spread of the agent	Conventional products in task performance	Poor working conditions	Task siting place
18	Trichloroethylene: Parkinsonism and complex 1 mitochondrial neurotoxicity	Degreasing metal parts	Trichloroethylene	Additional cases due to an environmental spread of the agent	Conventional products in task performance	Poor working conditions Processes developed improperly	Task siting place

Continued

19	Methemoglobinemia: an industrial outbreak among rubber molding workers.	Operators of steam presses to add adhesive in rubber strips for automobile bumper	Exposure (through manual handling) to an adhesive containing dinitrobenzene	-	Conventional products in task performance	Contaminated ancillary products	-
20	Cold blast furnace syndrome: a new source of toxic inhalation by nitrogen oxides	Recovery process of a "cold blast furnace"	Exposure to nitrogen oxides at high pressure and temperature	-	Maintenance tasks	-	Task sitting place
21	Epidemiologic investigation of respiratory morbidity at a nylon flock plant	Flocking tasks and cleaning residual flock	Nylon fibers and dust	-	Conventional products in task performance	Poor working conditions	Task sitting place
22	An epidemic of silicosis among former denim sandblasters	Denim sandblasting tasks	Silica	-	Conventional products in task performance	Poor working conditions	-
23	Group A streptococcal skin infection outbreak in an abattoir: lessons for prevention	Gutting (visceration) tasks	Lamb carcasses contaminated by streptococcus Group A	-	Conventional products in task performance	Poor working conditions	Task sitting place

(-) Non-reported.

Table 3. Synthesis of outbreak information regarding to occupational relationships (II).

Information regarding to occupational relationships (II)							
Ref.	Title	Task performed (relationship between cases)	Agent/risk exposure	Environmental spread	Exposure circumstances	Concurrent facts	Cases location
24	Hypersensitivity pneumonitis in a metal-working environment	Workers involved on processes that produce Microbial aerosols	MWF with bacterial and fungal contamination	Additional cases due to an environmental spread of the agent	Substances or ancillary products	-	Different sites in relationship to the tasks performed
25	An outbreak of extrinsic alveolitis at a car engine plant	Machine operators using MWF	Exposure to aerosols of contaminated MWF (Aspergillus and Penicillium)	Additional cases due to an environmental spread of the agent	Substances or ancillary products	-	-
26	Adverse skin reactions to personal protective equipment against severe acute respiratory syndrome—A descriptive study in Singapore	Workers caring for suspected or confirmed SARS patients	PPE N95 mask, (polypropylene)	-	Personal Protective Equipment	-	Different sites in relationship to the tasks performed (Departments of Emergency and Intensive Care)

Continued

27	Hypersensitivity pneumonitis due to metal working fluids: Sporadic or under reported?	Machine operators using MWF in three different automobile part manufacturing plants	MWF contaminated with mycobacteria	-	Substances or ancillary products	Innovation Processes	Different sites in relationship to the tasks performed
28	Aerosol mapping of a facility with multiple cases of hypersensitivity pneumonitis: demonstration of mist reduction and a possible dose/response relationship	Workers involved in different tasks, sharing the exposure to MWF in machining processes.	MWF mists	Environmental spread. No additional cases	-	Poor working conditions	Different sites in relationship to the tasks performed
29	An outbreak of occupational textile dye dermatitis from disperse blue 106	Workers wearing a working uniform	Dye disperse blue 106 and 124	-	Working uniform	-	-
30	Clinical investigation of an outbreak of alveolitis and asthma in a car engine manufacturing plant	Workers involved in the machining or washing of metal pieces operations	Exposure to aerosols of contaminated MWF (<i>Acinetobacter spp</i> and <i>Ochrobacter anthropic</i>)	Additional cases due to an environmental spread of the agent	-	-	Different sites in relationship to the tasks performed
31	An outbreak of occupational asthma due to chromium and cobalt	Workers involved in milling, turning and grinding metal pieces	MWF contaminated with chromium and cobalt	-	Substances or ancillary products	-	Different sites in relationship to tasks performed

(-) Non-reported (MWF) = Metal Working Fluid.

Finally, in a group of 4 of the 33 outbreaks analysed (**Table 5**), the main determinant of risk exposure showed an environmental nature due to contamination of the working environment. This environmental exposure prevailed over the exposure linked to the handling of both equipment and substances within the working process [40] [41] [42] [43].

In these outbreaks, cases were located in the contaminated places. One of the outbreaks occurred while working in a natural environment [41] and the remainder, in places located inside the plant [40] [42] [43].

In 2 of these outbreaks the exposure to physical contaminants was identified due to the proximity of radiant facilities [42] [43]. In one case, the workplace contamination had a chemical origin, as a result of usual operations in the working process [41]; another outbreak was due to contaminated walls [40]. As regards the concurrent facts in 2 of the outbreaks, poor maintenance jobs or

Table 4. Synthesis of outbreak information regarding to occupational relationships (III).

Ref.	Title	Information regarding to occupational relationships (III)					
		Task performed (relationship between cases)	Agent/risk exposure	Environmental spread	Exposure circumstances	Concurrent facts	Cases location
32	An outbreak of asthma in a modern detergent factory	Workers involved in packing tasks, production and distribution	Encapsulated enzymes (proteases, amylase and cellulase)	-	-	Innovation processes	-
33	Organic dust toxic syndrome at a grass seed plant caused by exposure to high concentrations of bio-aerosols	Reception and storage of seeds, handling of cleaning machines, working in proximity.	Grass seeds contaminated with endotoxins and microbial content	Additional cases due to an environmental spread of the agent	Raw material contaminated	-	Consecutive workplaces in relationship with the working process
34	Cluster of presumed organic dust toxic syndrome cases among urban landscape workers—Colorado, 2007	Mulch loading and unloading	Mulch dust contaminated by fungi, bacteria and endotoxins	-	Raw material contaminated	-	Consecutive workplaces in relationship with the working process
35	A cluster of leptospirosis among abattoir workers	Workers involved in several tasks in the abattoir process	Exposure to urine of Infected cattle	-	Raw material contaminated	-	Consecutive workplaces in relationship with the working process
36	Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant	Workers involved in mixing and packaging tasks	2,3-butanedione (flavor enhancer)	-	Additives to raw material	-	Consecutive workplaces in relationship with the working process
37	An outbreak of Pontiac fever due to <i>Legionella long beach</i> serogroup 2 found in potting mix in a horticultural nursery in New Zealand	Workers handling contaminated mulch	<i>Legionella long beach</i> serogroup	-	-	Poor working conditions	-
38	<i>Bacillus anthracis</i> contamination and inhalational anthrax in a mail processing and distribution center	Workers handling envelopes or involved in tasks of postal classification	Envelopes containing <i>B. anthracis</i> spores	Additional cases due to an environmental spread of the agent	-	-	Consecutive workplaces in relationship with the working process
39	Airborne irritant contact dermatitis and conjunctivitis after occupational exposure to chlorothalonil in textiles.	Workers involved in cutting, Sewing, or cleaning tent cloth	Chlorothalonil	-	Raw material contamination	-	-

(-) Non-reported.

Table 5. Synthesis of outbreak information regarding to occupational relationships (IV).

Ref.	Title	Information regarding to the occupational relationships					
		Task performed (relationship between cases)	Agent/risk exposure	Environmental spread	Exposure circumstances	Concurrent facts	Cases location
40	Q fever outbreak in industrial setting.	Office workers and workers setting on non-protected places	Dust containing <i>C. burnetii</i> spores	Additional cases due to an environmental spread of the agent	Removing contaminated straw boards from walls and ceilings	Office renovation works	Areas affected by dust from renovation works
41	Case report: three farmworkers who gave birth to infants with birth defects closely grouped in time and place—Florida and North Carolina, 2004-2005.	Working in tomato grower's farms	Exposure to pesticides during gestational period	-	-	Poor working conditions. Working in violation of the restricted interval entry	In grower field
42	Clustered outbreak of skin and eye complaints among catering staff.	Kitchen staff	UVC tubes	Additional cases due to an environmental spread of the agent	Electric fly killers	Incorrect maintenance (UVC tubes into electric fly traps)	Working areas next to UVC tubes
43	A cluster of male breast cancer in office workers.	Working office next to an electrical switchgear room	Electric-magnetic fields exposure	Additional cases due to an environmental spread of the agent	Electric facilities in the building	-	Working areas next to electrical switchgear room

(-) Non-reported.

poor prevention practices were documented [41] [42].

This appraisal allows synthesising the occupational outbreaks variability in 4 standard pathways of occupational outbreaks, with the following characterisation for 3 epidemiological components: technological linkage, spatial distribution and agent involved.

SPOO Type I (**Figure 2**).

- Technological linkage: Workers share the development of a specific operation within the working process, and may also be involved in maintenance operations of installations or machinery.
- Spatial distribution: Cases are located in the area where the activity is carried out, although in outbreaks due to airborne substances, nearby cases may appear as a result of an environmental spread.
- Potentially involved agents: These may be materials, substances, products or sub-products, specifically used to perform a particular task.

SPOO Type II (**Figure 3**).

- Technological linkage: Workers are involved in different tasks or operations,

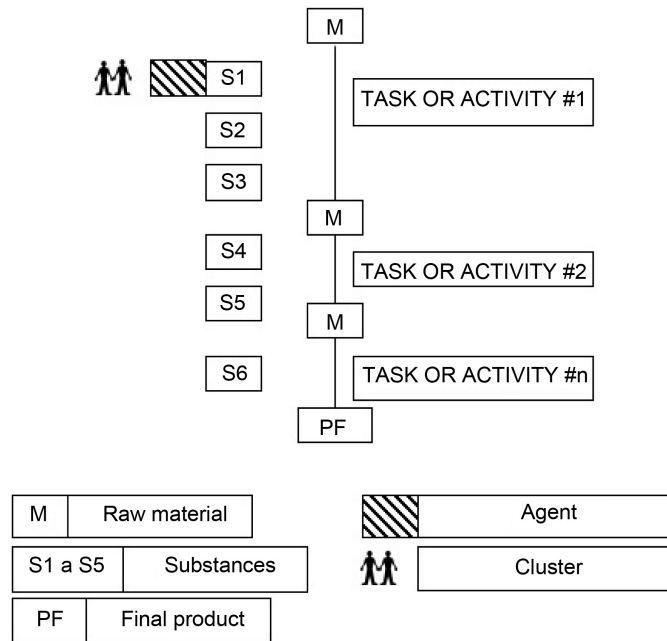


Figure 2. Standard occupational outbreak pathway Type I.

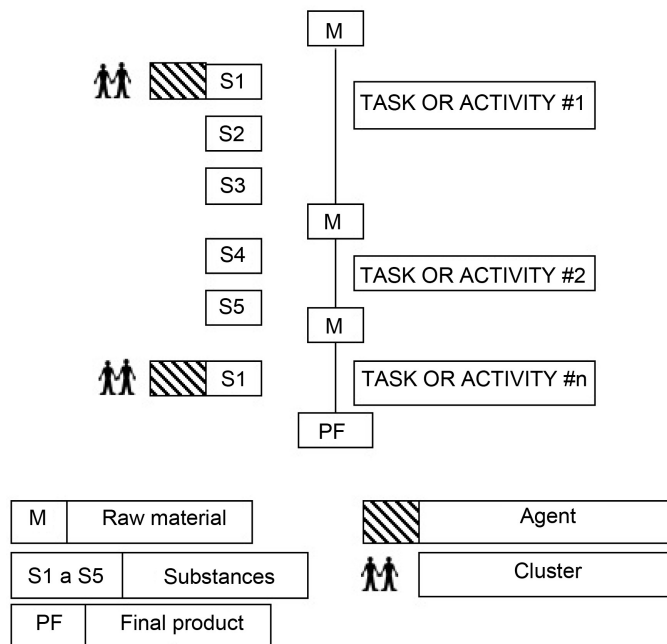


Figure 3. Standard occupational outbreak pathway Type II.

no consecutive in the work sequence. A common exposure is identified due to the use of the same product, substance or technology.

- Spatial distribution: Cases are located in the different areas where tasks or operations requiring the use of the causal agent are carried out. In outbreaks due to airborne substances, nearby cases may appear as a result of an environmental spread.
- Potentially involved agents: These may be substances, products, sub-products

or materials that are used at several points within the working process. Collective or individual protection equipment specifically used to perform those tasks may also be involved.

SPOO Type III (Figure 4).

- Technological linkage: Workers are involved in different consecutive tasks or operations within the working process.
- Spatial distribution: Cases are distributed throughout all or a part of the working process, according to the point where the causal agent appears. In outbreaks due to airborne substances, nearby cases may appear as a result of an environmental spread. The epidemic curve overlaps with the timing or sequence of the working process.
- Potentially involved agents: These may be the raw materials, substances or products which are incorporated into the raw material throughout the working process.

SPOO Type IV (Figure 5).

- Technological linkage: In this typology, the common exposure is due more to environmental than technological causes. The affected workers are related among themselves by sharing physical locations, rather than by the task performed or other technological reasons.
- Spatial distribution: Cases are located at specific places of the plant related to each other by architectural infrastructures, shared walls or places near to general equipment or facilities.
- Potentially involved agents: This epidemiological pathway stems from the spread of physical, chemical or biological contaminants from structural elements, walls, etc., emissions of contaminants from common workplace facilities or outdoor pollution.

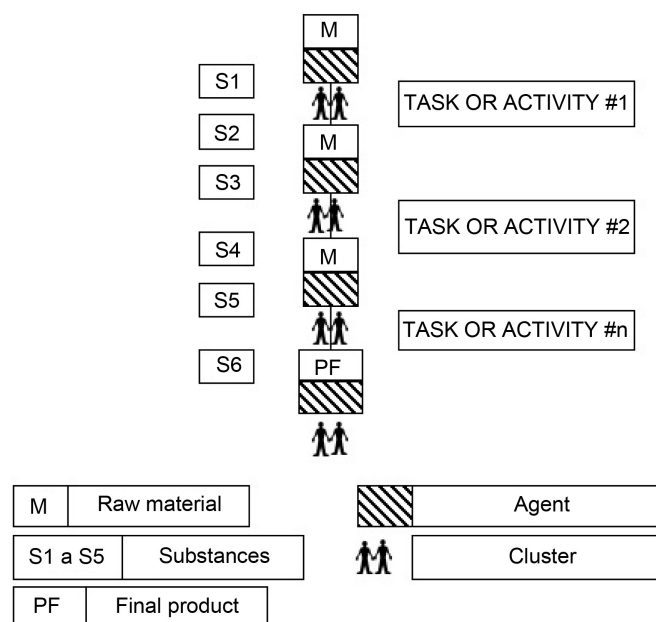


Figure 4. Standard occupational outbreak pathway Type III.

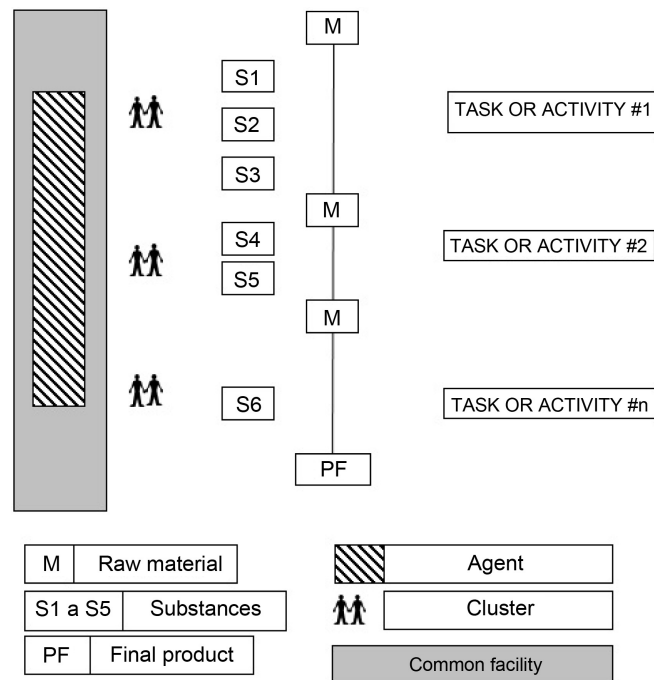


Figure 5. Standard occupational outbreak pathway Type IV.

Model's Adequacy: Homogeneity and Concordance between Components for Each SPOO

The analysis of 33 articles, used to formulate the theoretical SPOO (collection 1), and the 24 additional articles (collection 2) did not find any statistically significant differences as regards the probability of being classified in some one of the SPOO types (Table 6). There were no differences between the articles of collection 1 and 2 in order to be classified.

Out of the 57 outbreaks analysed, 53 (92.98%) were allocated to one of the 4 SPOOs. Only 4 outbreaks did not meet the criteria to be allocated to one of them.

In order to consolidate the theoretical models, it is relevant to test the association and concordance between components for each pathway type.

For this analysis, a selection was carried out of 36 outbreaks documented in the three components under study.

(Table 7) shows a significant association between all three epidemiological components (technological linkage, spatial distribution and potentially involved agents) for each theoretical pathway type (Fisher's exact test $p < 0.001$).

The concordance analysed by the Kappa index shows no discordance among the three components of SPOO Type II ($Kappa = 1$). An almost perfect concordance was found among the components of SPOO Type IV ($Kappa_{\text{Technological linkage/Spatial distribution}} = 0.93$; $Kappa_{\text{Technological linkage/Agent involved}} = 0.94$; $Kappa_{\text{Spatial distribution/Agent involved}} = 0.87$).

For SPOO Type I (Table 7), the Kappa index showed an almost perfect concordance between technological link and spatial distribution

Table 6. Difference in the level of allocation among the occupational outbreak collections under study.

	Outbreaks allocated due to the concordance of 3 criteria	Outbreaks allocated due to the concordance of 2 criteria	Not allocated	Total	Sig. F (p)
Collection 1 (articles used to formulate the pathways of occupational outbreaks)	18	14	1	33	0.407
Collection 2 additional collection	13	8	3	24	
Total	31	22	4	57	

($Kappa_{\text{Technological linkage/Spatial distribution}} = 0.94$), a strong concordance between technological link and agent involved ($Kappa_{\text{Technological linkage/Agent involved}} = 0.66$), showing a moderate concordance between spatial distribution and agent involved ($Kappa_{\text{Spatial distribution/Agent involved}} = 0.87$).

There was a strong concordance among the components of SPOO Type III, between technological link and agent involved ($Kappa_{\text{Technological linkage/Agent involved}} = 0.68$), as well as between spatial distribution and agent involved ($Kappa_{\text{Spatial distribution/Agent involved}} = 0.68$). No discordance was found between technological link and spatial distribution ($Kappa_{\text{Technological linkage/Spatial distribution}} = 1$) (Table 7).

A sub-sample of 36 outbreaks, fully documented in all three components, was analysed by calculating conditioned probability that allows to identify both the global behaviour of an outbreak and the behaviour of each component (Table 8).

Since the outbreak investigation started by getting to know the “Spatial distribution of cases”, the most likely epidemiological scenarios are Type I ($p = 0.36$) and Type IV ($p = 0.28$).

Outbreaks classified as Type I showed a variability regarding the “Technological linkage”. In spite of this, the most probable behaviour ($p = 0.92$) for this component was the one expected for that theoretical model.

Outbreaks classified according to their spatial distribution as Type II, Type III and Type IV showed, in its three components, a total concordance to the theoretical models.

Analysing the outbreak pathways by calculating variations with repetition of four elements (Type I, II, III and IV) taken in threes (technological linkage, spatial distribution and agent involved) make a total of 64 possible pathways.

The 36 outbreaks analysed (fully reported regarding the three components) show that, out of those 64 possible pathways, only 7 really happened (Table 9).

Table 7. Homogeneity and concordance between components of the standard pathways of occupational outbreaks.

Components of analysed outbreaks	Theoretical Outbreak pathway Type I			Sig. F (p)	Kappa (p)
	Spatial distribution Type I	Spatial distribution Types II, III, IV	Total		
Technological linkage Type I	12	0	12		
Technological linkage Types II, III, IV	1	23	24	<0.001	0.94
Total	13	23	36		
Components of analysed outbreaks	Agent involved Type I	Agent involved Types II, III, IV	Total	Sig. F (p)	Kappa (p)
Technological linkage Type I	7	5	12		
Technological linkage Types II, III, IV	0	24	24	<0.001	0.66
Total	7	29	36		
Components of analysed outbreaks	Agent involved Type I	Agent involved Types II, III, IV	Total	Sig. F (p)	Kappa (p)
Spatial distribution Type I	7	6	13		
Spatial distribution Types II, III, IV	0	23	23	<0.001	0.60
Total	7	29	36		
Components of analysed outbreaks	Theoretical Outbreak pathway Type II			Sig. F (p)	Kappa (p)
	Spatial distribution Type II	Spatial distribution Types I, III, IV	Total		
Technological linkage Type II	7	0	7		
Technological linkage Types I, III, IV	0	29	29	<0.001	1
Total	7	29	36		
Components of analysed outbreaks	Agent involved Type II	Agent involved Types I, III, IV	Total	Sig. F (p)	Kappa (p)
Technological linkage Type II	7	0	7		
Technological linkage Types I, III, IV	0	29	29	<0.001	1
Total	7	29	36		
Components of analysed outbreaks	Agent involved Type II	Agent involved Types I, III, IV	Total	Sig. F (p)	Kappa (p)
Spatial distribution Type II	7	0	7		
Spatial distribution Types I, III, IV	0	29	29	<0.001	1
Total	7	29	36		
Components of analysed outbreaks	Theoretical Outbreak pathway Type III			Sig. F (p)	Kappa (p)
	Spatial distribution Type III	Spatial distribution Types I, II, IV	Total		

Continued

Technological linkage Type III	6	0	6		
Technological linkage Types I, II, IV	0	30	30	<0.001	1
Total	6	30	36		
Components of analysed outbreaks	Agent involved Type III	Agent involved Types I, II, IV	Total	Sig. F (p)	Kappa (p)
Technological linkage Type III	6	0	6		
Technological linkage Types I, II, IV	4	26	30	<0.001	0.68
Total	10	26	36		
Components of analysed outbreaks	Agent involved Type III	Agent involved Types I, II, IV	Total	Sig. F (p)	Kappa (p)
Spatial distribution Type III	6	0	6		
Spatial distribution Types I, II, IV	4	26	30	<0.001	0.68
Total	10	26	36		
Theoretical Outbreak pathway Type IV					
Components of analysed outbreaks	Spatial distribution Type IV	Spatial distribution Types I, II, III	Total	Sig. F (p)	Kappa (p)
Technological linkage Type IV	10	1	11		
Technological linkage Types I, II, III	0	25	25	<0.001	0.93
Total	10	26	36		
Components of analysed outbreaks	Agent involved Type IV	Agent involved Types I, II, III	Total	Sig. F (p)	Kappa (p)
Technological linkage Type IV	11	0	11		
Technological linkage Types I, II, III	1	24	25	<0.001	0.94
Total	12	24	36		
Components of analysed outbreaks	Agent involved Type IV	Agent involved Types I, II, III	Total	Sig. F (p)	Kappa (p)
Spatial distribution Type IV	10	0	10		
Spatial distribution Types I, II, III	2	24	26	<0.001	0.87
Total	12	24	36		

Source: 36 outbreaks, fully documented in all three components under study.

Table 8. Probability of occupational outbreak pathway. The investigation starts by analysing the spatial distribution of cases.

	Outbreak components		
	Spatial distribution (p/n)	Technological linkage (p/n)	Agent involved (p/n)
			Type I (p = 0.58/n = 7)
	Type I (p = 0.36/n = 13)	Type I (p = 0.92/n = 12)	Type III (p = 0.33/n = 4)
			Type IV (p = 0.08/n = 1)
OUTBREAK		Type IV (p = 0.08/n = 1)	Type IV (p = 1.00/n = 1)
	Type II (p = 0.19/n = 7)	Type II (p = 1.00/n = 7)	Type II (p = 1.00/n = 7)
	Type III (p = 0.17/n = 6)	Type III (p = 1.00/n = 6)	Type III (p = 1.00/n = 6)
	Type IV (p = 0.28/n = 10)	Type IV (p = 1.00/n = 10)	Type IV (p = 1.00/n = 10)

Source: 36 outbreaks, fully documented in all three components under study.

Table 9. Pathways of occupational outbreak: occurrence probabilities.

Standard pathways: occurrence probabilities			
Spatial distribution	Technological linkage	Agent involved	p
Type IV	Type IV	Type IV	0.28
Type II	Type II	Type II	0.19
Type I	Type I	Type I	0.19
Type III	Type III	Type III	0.17
Not-standard pathways: occurrence probabilities			
Type I	Type I	Type III	0.11
Type I	Type I	Type IV	0.03
Type I	Type IV	Type IV	0.03

Source: 36 outbreaks, fully documented in all three components under study.

The most probable ones were those which behaved exactly like the model (83%).

4. Discussion

The investigation of an occupational outbreak, once the index case has been identified, triggers a stress situation between the company's social agents, who exert great pressure on epidemiologists. This fact, together with the variability of the possible causes, makes the first steps to investigate the outbreak particularly difficult. The lack of knowledge about the working process, the social climate, the disorientation and the uncertainty stress the field epidemiologist.

Occupational epidemiology shows differential facts inherent to the work environment. Exposure to risk at the workplace is generally known. But a situation which is not common in public health epidemiology and which needs a new element is "the technology used in working processes". This element causes an exposure which varies according to the working process or work sequence, in such a way that the epidemic curve depends on the tasks performed at each

moment of the work process or sequence and produces a differentiable epidemiologic behaviour.

In this sense, a critical and in-depth evaluation of the 33 occupational outbreaks reported in scientific journals and the analysis of three parameters epidemiologically similar (link between cases and working process, spatial distribution and exposure to agents or risks involved), allows to corroborate the hypothesis that the variability of occupational outbreaks can be normalised in four standard pathways (Types I, II, III and IV) where a differential and proper epidemiological behaviour has been demonstrated regarding the link with the working process, the distribution of cases and the potentially involved agents.

Results are also conclusive as regards approaching the study of epidemic outbreaks in work environments on the basis of the distribution of cases within the company. This aspect is decisive in behaviours of Types II, III and IV.

Results are also conclusive as regards the best way to approach the investigation of an epidemic outbreak in the work environment. The early awareness of cases distribution within a company is an epidemiological dimension that is vital to identify the suspected causal agent, mainly in pathways Types II, III and IV.

The most frequent epidemiological pathway in occupational outbreaks is Type I. This means outbreaks that affect workers who perform together a specific task within the working process, located in the area where the activity is carried out and caused by materials, substances, products or by-products used specifically to perform a particular task. And also Type IV, which means outbreaks which are more due to environmental than technological causes. Their origin is linked to the spread of physical, chemical or biological pollutants from structural elements or common work facilities.

It was impossible to assign a typology in 4 outbreaks, either because the publication did not provide information on two or more components [41] [44] [45] or because at least two components showed a behaviour different from the expected one according to the theoretical pathway [46].

The analysis of the 36 outbreaks that are fully documented regarding the three components (technological linkage, spatial distribution and agent involved) has shown their epidemiological trajectory. The probability that a given outbreak would fit its three components into any of the four theoretical pathways was 0.83.

The outbreaks classified as Type II, III and IV show a full concordance with the theoretical itinerary.

5. Conclusion

The results corroborate the hypothesis where the occupational outbreaks present a limited variability, allowing them to be categorized into a theoretical model of 4 standard occupational outbreak pathways. The incorporation of those pathways to the field of occupational epidemiology will allow, just by being allocated to one of them: 1) to provide early guidance to epidemiological, clinical and en-

vironmental studies focused on the specific hypothesis of causality; 2) to anticipate preventive measures and 3) to contribute to an earlier and more efficient outbreak resolution.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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