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Graph Theory Applications to Comprehend Epidemics Spread of a Disease

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Abstract: *Theory of Graphs could offer a plenty to enrich the analysis and modelling to generate datasets out of the systems and processes regarding the spread of a disease that affects humans, animals, plants, crops etc., In this paper first we show graphs can serve as a model for cattle movements from one farm to another. Second, we give a crisp explanation regarding disease transmission models on contact graphs/networks. It is possible to indicate how a regular tree exhibits relations among graph structure and the infectious disease spread and how certain properties of it akin to diameter and density of graph, affect the duration of an outbreak. Third, we elaborate on the presence of a suitable environment for exploiting several streams of data such as genetic temporal and spatial to locate case clusters one dependent on the other of a disease that is infectious. Here a graph for each stream of data joining all cases that are created with pairwise distance among them as edge weights and altered by omitting exceeding distances of a cut-off assigned that relies on already existing assumptions and rate of spread of a disease information. Fourth we provide an overview of epidemiology, disease transmission, fatality rate and clinical features of zoonotic viral infections of epidemic and pandemic magnitude since 2000. Fifth we indicate how the clinical data and virus spread data can be exploited for the creation of health knowledge graph. Graph Theory is an ideal tool to model, predict, form an opinion to devise strategies to quickly arrest the outbreak and minimize the devastating effect of zoonotic viral infections.*

Keywords: *Virus, Epidemics, Pandemics, Graph, Regular Tree.*

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1. Introduction

It is easy to notice a lot of sheep and cattle while travelling along the countryside of any country. A vast amount of data is collected and recorded regarding their management including its routine of movements from farms to markets and vice-versa. Epidemiologists as a group realized that cattle movements can be thought of as a graph and this visualization could help to detect and control among them the possibility of a disease spread. It is usual to record cattle movements from one agricultural holding to another and are reported to government build a central database to mathematically model infectious disease spread of cattle and to monitor the operation of the agriculture industry as a wholesome. Due to pertinence of animal loitering in common disease outbreaks such as mouth-foot disease a huge amount of modeling work is done from the perspective of network science regarding how one can incorporate temporal information into such a graphical representation.

1.1. Graph as a Model for Movements

The dataset about cattle roam record register maintain roam records for each animal, including their births and deaths. A graph evolves by taking each farm as a vertex and an edge is introduced from one farm to another if there is trade or animal loiter among them within a given time span. This graphical formulation way gives huge information concerning their contact time, weight, and direction. Such a graph can be thought of as a directed, weighted, or temporal graph.

If only a small number of auction markets are involved in cattle trade business, then the graph representing it will have farms and markets alone in the vertex set. So, number of vertices (the markets) is less but some of the vertices may have high degree, and some of them may have comparatively low degree. This structure will resemble a hub-and-spoke-like graph. Such structures provide quick easy solutions to many computationally difficult problems but not necessarily apt for each setting of a disease. A disease that is propagating at a slower rate may require close contact to spread and hence market may not be required. In that case one considers a market-san version of the graph in which an edge from one vertex to another shows only an animal loiter.

However, ignoring the information that is temporal while forming a cattle loiter data induced graph, may result in distorted view of transmission pathways of disease. The cattle trade timing is pertinent in disease modelling. For instance, consider P3 (a path of length 2 on 3 vertices), with all possible edge ordering. That is, let us deem that first in the path x-y-z, the edge (x, y) occurs first and then the edge (y, z) and in the second case the edge (y, z) occurs first and the edge (x, y) occurs next. In the case of former we deem an infection spread from x to z, and a path, x-y-z is temporally admissible, in the case of the latter it is not. So, in a time-neglecting scenario with dataset of more than a cattle loiter data record for a week, half of the P3's is temporally feasible when time factor is included. This aspect has resulted in the wide knowhow of graphs that are dynamic and temporal in the context of graph algorithmic treatment and in the science graphs/networks.

By a graph in temporal sense we mean, $G = (V, E, \Delta)$, a triple with vertex set V and edge set E and $\Delta: E \rightarrow T$, a function with T a set of time steps. Here $\forall\ e \in E$, $\Delta(e)$ denotes time steps. One can allow a weighted/temporal graph by letting G as so. As there are several tools available to deal static graphs, attempts are made to make it dynamic in static graphs. One can see (Vernon & Keeling, 2008) for more. In Kim and Anderson, 2012 a static & directed network is suggested in which V(G) is multiple copies of vertices, with appropriate vertex duplication at all appropriate time step, and edges pointing forward in time. In (Heath et al., 2008) the authors made quick use of a line graph model to catch information concerning a disease's infection period to form a graph that is static which provides vital information that is dynamic. In this graph, the vertex set comprise trade and days at which they happened and an edge is introduced between two vertices if disease spreads from one trade/time pair to another in the first instance and could move over to the second subsequently.

Mathematically, from a given digraph $G = (V, E, \Delta)$ that is temporal along with δ_I (period of infection), a new digraph $H = (U, E_1)$ is formed with $U = \{(e, t),\ e \in U \text{ and } t \in \Delta(e)\}$, and $E_1 = \{((e, t_e) \rightarrow (f, t_f)) \text{ where } e = (u, v)$ and $f = (v, w)\} \leftrightarrow te < T(f), t_f - t_e \leq \delta_I$. Here the static representation brings out the directionality of the original graph as well as time.

2. How to reduce the disease spread?

A high volume of previous research available in literature has indicated that the strategic omission of pertinent high degree vertices representing dealers or markets or the edges with several measures is more productive in lowering the size in a simulated disease outbreak. This act is preferred more to omission of farms that is random. The authors in (Gates & Woolhouse, 2015) provide supporting document by indulging in edge centrality, measure that is simple. They pick a high potential disease spread edges from a graph/network and rebuild by employing a process that is matching specific and heuristic and the one that preserves in/out degree.

This method provides networks with reduced prevalence of endemic disease compared to real-data networks. That is, when a graph with a budget provision is given for vertex/link omission, what could be a wise option? The reference (Enright &, Meeks, 2018) concentrates on omitting edges to reduce the size of a maximum connected component so that it serves as a maximum allowed limit for a huge outbreak.

2.1. Contact Networks

We have huge responsibility to prepare societies and spare further harm through mathematical models of different disease scenarios and contribute to better knowhow of disease dynamics and develop course of action like quarantine or vaccinations that is effective control specific (Just et al., 2015). Contact networks can be thought of as Graphs that stands for disease interaction are deemed as contact networks. Here nodes indicate to persons and two nodes are joined when there is a chance them to communicate. For instance, a crop field could be a grid shaped graph that acts as a model for swarms (due to insect) affecting the crop (Keeling & Eames, 2005). A better representation for contact networks is through regular tree graphs (ie, graphs that are connected and acyclic with same number of edges for all its vertices). Tree graphs due to san of loops are sought after representation for SARS like outbreaks (Riley et al., 2003). For improving the reliability criteria of such networks one can refer to (Beiu et al., 2017; Rohatinovici et al., 2018). Instances of trees like structure are seen in systems such as the cardiovascular. Disease analysis is a first forward step on this type of graph to deeper and natural knowhow of it spread.

It is important to keep in mind that a tree graph with equal number of incident edges for all its vertices gives a type of made easy structure to notice outbreak spread pattern on a network of disease contact. Pathogens and infectious hosts are mostly the cause for the dangerous outbreak that agrees aptly with network of disease contact. For instance, consider the information drift in an organization, where the CEO acts as the root and hence has links to various standalone divisions. Each division head passes the conveyable through his subordinate. An ‘outbreak’ of an order could trigger at the root and possess high probability of spreading. One can identify a human/rat infection spread via land route through various means. Genetic disorders akin to color blindness or cystic fibrosis that are hereditary can also cause outbreaks on networks that are tree structured. The height of the graph also plays a crucial role in finding the outbreak duration.

We define the height λ of a tree as the farthest distance from the root vertex to any other vertex. It is easy to observe that if T is a regular tree with p vertices then $p = \sum_{n}^{\lambda} d^{i}$ and d stands for degree of a vertex. Moreover, the parameters λ and d of graphs behave in a specific manner based on the size of the threshold (Seibold & Callender, 2016) found that d has slight effects when λ improves the chance of spread of an infection required for causing a disaster at a deceasing rate. This paves way for not only to foresee the threshold for tree graphs with equal number of incident edges for all its vertices, but also to foresee the threshold on tree graphs with unequal number of incident edges for all its vertices. Irregular graphs are apt to mimic contact type networks that lack the symmetry. Irregular trees with unequal number of incident edges for all its vertices have a smaller number of vertices than a regular tree with equal number of incident edges for all its vertices with equal λ and d. With lesser vertices and edges, the infection spread rate on an irregular tree are more prone to follow infection spreading rate on a regular tree graph with given λ and d. The behavior of a regular tree with equal number of incident edges for all its vertices could be of the maximum duration and final size of an outbreak on a graph structure with equal number of incident edges for all its vertices. The authors in (Seibold & Callender, 2016) did a matching work of the knowing the differences in vertex set size and the imminent outbreak duration and among the two types of graphs the final size.

3. Detecting Outbreak Clusters

Disease outbreaks that are infectious form a repeating menace both to animals and humans. It has devastating effect on all aspects of biodiversity, health and economy. Major epidemics like the influenza pandemic of 2009 (Fraser et al., 2009), MERS-the Middle-East Respiratory Syndrome (Bauch & Oraby, 2013; Cauchemez et al., 2014) and the EVD-Ebola virus disease of West-Africa outbreak (Kreuels et al., 2014) reiterated the pertinence of early stage outbreak assessment. The best strategy to contain it is fast determination of cases forming clusters and mitigation follow up of the strategy to contain the epidemic spread.

The bringing out of cases forming clusters is an adopted tactics to defeat the ongoing slaughter of epidemics. A fair valuation of benefactions of local transmission vs importation of case is irredundant for designing apt intercession plan of action. For example, an outbreak of nosocomial type may be due to transmissions in a hospital or from the community induced instigations, asking for control measures (Harris et al., 2013; Chung et al., 2015; Cauchemez et al., 2013). Likewise, local transmissions and magnitude of cases from other places/nations demand control measures of varying nature, such as anticipation and social distancing vs closing of borders (Cauchemez et al., 2016; Koopmans et al., 2004). If occurrence of zoonotic infections take place then locate the compass to which channelling within-species and reservoir divulge accord to the descry prevalence, as explained in the case of avian influenza (Koopmans et al., 2004; Ferguson et al., 2004), bovine tuberculosis (Donnelly & Nouvellet, 2013) or MERS (Cauchemez et al., 2013; Cauchemez et al., 2016).

We now see a framework for adjoining different provenance of information to locate cases leading to cluster formation of a disease. This approach based on corroboration coalescence can put forth into one numerous data stream like the prearrange and locale of the cases and WGS of the pathogen to point clusters forming outbreak. This way anticipates on the fact that persons in an outbreak who infect each other possess fair chance of being closely related with known characteristics. For example, the onset of their symptom happens within the identical period and in neighbouring locale and exhibit genetically identical pathogen strains. One can deem it to belong to same cluster of outbreaks, closely matching in all apposite data streams. These data origins narrate links between cases in varying spaces such as genetic, spatial and profane but all be put forth to determine pairwise distances between cases like number of days elapsed between various dates of onset, geographic distance between locations, number of mutations between pathogen WGS etc. One can define for each such data stream a weighted graph where vertices correspond to cases and the edge between two cases is weighted by the brace distance between two cases so that noticeable edges denote brace of cases with no chance to have infected one another. Then to consider only apropos links every graph is sheared by deleting identified edges whose weight is greater than a preset check distance.

Setting the ample check is crucial to locate related cases forming clusters. Cori et al, 2018 introduced a skeleton for setting check depending on the contemplated distance distributions among perceived cases in an outbreak. This enabled them to consider pre-living counsel about a disease. That is, the prorating of its ensuing time elapsed from onset of symptoms in a person and his/her infector, its spatial kernel, and its rate of mutation. This counsel is available for thoroughly checked outbreaks which is not possible in practice to be the case. To resolve this underreporting is a right approach to be followed. They gave answer to the anticipated distances among watched cases for a pre-set level of announcing as well as some inquisitive results for common issuance wielded to describe distances among cases in time and space. Every trimmed graph point to epidemiological links among cases for assumed data origin. To amalgamate these pieces of counsel, they merged the trimmed graphs through intersection. This makes the resulting connected components of the eventual graph mark clusters of cases corroborated for all data type. The ensuing clusters point to all possible cases dappling to the same channelling tree. Mainly the sizes of the clusters also comprise counsel about the underlying channelizing (Cauchemez et al., 2013). The authors in (Cori et al., 2018) exploited this counsel by deriving reckons of the duplication number, R given the factual issuance of the cluster sizes and the surmised reporting rate.

4. Viral Infections of Epidemic Magnitude Since 2000

In what follows we are going to give a bird's eye view of different zoonotic viral infections since 2000 and how they blossomed into epidemic proportion. In Figure 1 we give a Flow chart view of zoonotic animal-borne and vector-borne viral transmission to human species causing disease outbreaks. In Table 1 we provide the details of epidemiologic features, disease transmission and fatality rate of emerging viral infections. In Table 2 we give a comparison of common clinical features of all the viral epidemics. In Table 3 we bring forth explicitly other cautioning symptoms of clinical nature. One can see WHO Ebola Response Team, 2015; World Health Orhanization, 2018b; Hamidouche, 2020; World Health Orhanization, 2018a; World Health Orhanization, 2020a; 2020b; World Health Orhanization, 2018c; Centers for Disease Control and Prevention, 2019; 2015 Indian Swine Flu Outbreak, 2020; Bennett & Domachowske, 2020; Noor & Ahmed, 2018; PAHO & WHO Data", 2019; World Health Orhanization, 2017; 2020c) for a very crisp informative literature on various viral infections that assumed epidemic spread and some of it even became pandemic. Although a number of calculus centric mathematical methods are available in literature to mathematically model the virus spread, a mathematical model which discrete in nature and still serve as a good model like any other is available with Graph Theory.

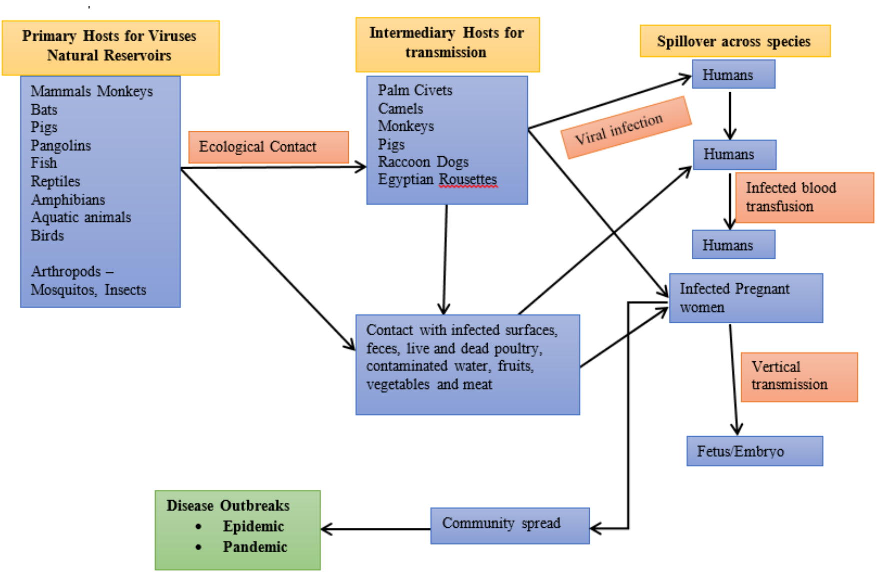

Figure 1. Flow chart of zoonotic animal-borne and vector-borne viral transmission to human species causing disease outbreaks

Source: Authors' own conception

Table 1. Details of epidemiologic features, disease transmission and fatality rate of emerging viral infections *(authors' own contribution)*.

Viral infections	Family	Natural reservoirs	Intermediate host	Origin	Period of outbreak	Outbreak status	Total number of reported case	Fatality rate
SARS	Coronoviridae	Chinese rufous horseshoe bat	Palm civets, raccoon dogs	Foshan, China	2002-2003	Epidemic	8,096	9.6%
MERS	Coronoviridae	bats	camels	Jeddah, Saudi Arabia	2012-2018	Epidemic	2,229	35.5 %
Covid-19	Coronoviridae	Bats, Pangolins	unknown	Wuhan, China	2019-Present	Pandemic	1,773,084*	2.55 %
Nipah virus	Paramyxoviridae	Flying foxes,	Infected food	Kerala, India	2018	Epidemic	700	40-70%

		fruit bats, Pigs						
Ebola virus	Filoviridae	Fruit bats	Monkeys, pigs, bats infected surfaces	West Africa Democratic republic of Congo	2014-2016 2020	Epidemic	28,616 3,453	50% 66%
Marburg virus	Filoviridae	Fruit bats	Egyptian rousettes	Equatorial Africa	2007-2017	Endemic	26	100%
Swine flu (H1N1)	Orthomyxoviridae	Swine	Contaminated environment, poultry	United States India	2009-2010 2014-2015	Pandemic Epidemic	60.8 Million 33,761	1-4% 6.03%
Avian Flu (H5N1) **(H7N9)**	Orthomyxoviridae	Aquatic birds, Pigs	Contaminated environment, poultry	Hong Kong China	2003 2013-2017	Epidemic	844 631	60% 30%
Zika Virus	Flaviviridae	*Aedes* Mosquitoes	Mosquito-Monkey-Mosquito	Brazil	2015-2016	Epidemic	976,235	8.3%
Chikungunya	Togaviridae	*Aedes* Mosquitoes	-	Africa	2014-present	Epidemic	1.8 million	<1%
Dengue	Flaviviridae	*Aedes* Mosquitoes	-	Asian and Latin America	2014-present	Epidemic	100-400 million/ year	<1%

*data obtained as of 13th April 2020 published by WHO; Superscript numbers denote the references.

Table 2. Comparison of common clinical features of all the viral epidemics

Source: Authors' own conception

Clinical characteristic	**Covid-19**	**SARS**	**MERS**	**Ebola**	**Marburg**	**Swine flu**	**Avian flu**	**Nipah**	**Dengue**	**Chikungunya**	**Zika**
Fever	+++	+++	+++	+++	+++	++++	++++	+++	++++	+++	++

											+
Cough	++++	++++	++++	+++	+++	+++	+++	-	-	-	-
Sneezing	-	-	-	-	-	+++	+++	-	-	-	-
Sore Throat	++++	++++	++	+++	+++	++	++	-	-	-	-
Diarrohea	++	+++	++	+++	+++	+++	+++	-	-	-	-
Vomiting and Nausea	++	++	++	++	++	+++	+++	-	++	++	+
Decreased appetite	-	-	-	-	-	+++	+++	-	-	-	-
Weakness & Weight loss	-	-	-	++	++	+++	+++	-	++	++	++
Headache	-	-	-	+++	+++	+++	+++	+++	-	-	-
Drowsiness & Mental confusion	+++	++	+	-	-	++	++	+++	-	-	-
Shock	-	-	-	-	-	+++	+++	++	-	-	-
Skin rashes	-	-	-	++	++	-	-	-	+++	+++	-
Conjuctivitis	-	-	-	++	++	+	+	-	-	+++	++
Pain in joints and back	-	-	-	++	++	-	-	-	+	++++	+++
Body pain	-	-	-	+	+	+++	+++	-	+	++	+
Abdominal pain	-	-	-	++	++	+++	+++	-	-	-	-
Shortness of breath /Breathing difficulty	+++	+++	++	-	-	++	++	+++	+	+	+

Here +/- denotes the presence / absence of the symptoms for each viral infections. The double or triple '+' signs indicate the frequency of symptoms
Source: Authors' own conception

Table 3. Other cautioning clinical ailments
Source: Authors' own conception

Viral Infections	Diseases
Covid-19 **SARS** **MERS**	ICU admission Ventilator support Acute Respiratory Distress Syndrome Pneumonia Kidney Injury Thrombocytopenia Leukopenia Lymphopenia
Nipah virus	COMA Encephalitis
Ebola virus **Marburg Virus**	Maculopapular rash Severe bleeding in the eyes and mucus membranes, Gastrointestinal tract, stools Hematoma Low Blood Pressure
Swine flu **Avian flu**	Severe pneumonia Acute Respiratory Distress Syndrome Encephalitis Multiorgan dysfunction Hypoxemic respiratory failure
Dengue **Chikungunya** **Zika virus**	Accumulation of fluid with respiratory insufficiency Severe bleeding Dengue Shock syndrome Polyarthralgia Arthritis Maculopapular rashes Hepatomegaly Seizures in children Periarticular edema Microcephaly Guillain-Barre Syndrome

5. Knowledge Graphs on Clinical Data

Network The flourishing graph model has shown its significance as a diagnostic measure by creating a link between disease and its set of symptoms. Exploiting Google as an information retrieval gateway, the

Google health knowledge graphs can be created for every kind of contagion by retrieving medical records and related information online. This Google health knowledge graph was developed in 2015 through a multi-step procedure fastening techniques of data mining with the help of manual curators to assist patients with their medical conditions. This graph is intended for patients who are looking for health related queries from Google which strictly appears only to the users of US, Brazil and India. One can see (Rotmensch et al., 2017) for more. Knowing the knowledge graph comprises three critical steps. 1] Compilation of reports from positively tested disease and its symptoms from structured and unstructured inputs, 2] construction of statistical models for developed disease and symptoms, 3] development of knowledge graphs from the conceived data of statistical models. One may build a pertinence measure for every model to find out if an edge should be drawn between vertices denoting disease and symptom as this pertinence measure specifically tags the model's relative confidence that an edge must exist or not. Based on this pertinence measure one can group the symptoms of the disease. Hence, we suggest that the clinical data given here in Section 4 could be exploited for the creation of a health knowledge graph. One has to keep in mind the following eight uphill tasks while forming a health knowledge graph based on clinical data. a) Understanding the impact of diversity on parameter estimation and epidemic outcome, (b) Developing analytical methods for studying epidemics based on static un-weighted knowledge graph, (c) Establishing analytical methods for modelling weighted and dynamic knowledge graph and epidemics thereon, d) Incorporating diminishing immunity in knowledge graph epidemic models, e) Developing and validating approximation schemes for epidemics on knowledge graphs, f) Illustrating the influence of knowledge graph properties on the outcome of an epidemic, g) reinforce the correlation between knowledge graph modelling and epidemiologically available data, and h) Design knowledge graph-based interventions. To explore the spread and management of contagious diseases in a closed population the authors introduced a new knowledge graph (Ancel Meyers et al., 2003). As the outbreaks occur in a closed or semi-closed environment, such epidemic conditions are hard to contain or manage due to delays in disease spotting and the long incubation period of the bacterium. One such case is the pneumonia caused by Mycoplasma pneumonia. This model clearly describes the dynamics of interactions between patients and caretakers. Despite the reduced incidence of Mycoplasma pneumonia found amongst caretakers, this health knowledge graph suggests the degree to which these caretakers are secured against infections which are central to the management of mycoplasma epidemic.

6. Conclusion

Through Graph theory plays a pivotal role in exploring and understanding the procedures that generates statistics. Graphs that result out of modelling from geographical nearness are mostly planar. One can do a plenty of work on optimization problems linked to agriculturally derived graphs. We could see a spike in the development of the algorithmic studies of temporal graphs in the literature. A regular tree graph is a good model to probe trends in the evolution and progression of epidemic outbreaks on a contact network. Hereditary genetic disorders like colour blindness, cystic fibrosis or ALS on a contact network can be represented as tree networks to describe an outbreak. As the human species are susceptible to the infections and can be infested at several points of time generating several loops, the tree network generates a clear, uncomplicated structure for observed sets of symptoms. A standard graph is an excellent parameter to determine the duration of an outbreak. To conclude, each animal is a host of various virus strains, and the virus richness varies between different species. Since the outbreak of novel Corona virus, zoonotic viruses that cause 60-80% deadly infections in humans and animals has been a greater importance of research in medical science. These newly arising and resurfacing viral infections insist a great risk to global public health. Some of the zoonotic animal-borne viral epidemics that caused world-wide menace include Avian Influenza virus (H5N1, H7N9), Swine influenza virus (H1N1), Corona virus (SARS (Severe Acute Respiratory Syndrome), MERS (Middle East Respiratory Syndrome) and the novel Covid-19), Henipa virus (Nipah), Ebola virus, Marburg virus and some zoonotic vector-borne viral infections include Zika virus, Chikungunya and dengue. Ever since the discovery of coronavirus, scientists have been cautioning that some of them are uniquely related to cause human pandemics and today we find such a case, the novel covid-19. Graph Theory is really a good tool to model, predict, form an opinion to devise strategies to quickly arrest the outbreak and minimize the devastating effect of zoonotic viral infections. The authors in (Rotmensch et al., 2017) noted that a good quality health knowledge graph can be built from the medical records achieved electronically from the health care providers. This ideal health knowledge graph proved to be an exactitude model with their two-step methods just by correcting a few of the edges as proposed by the model. Reviewing the outcomes of the clinical assessment, one may conclude that if a correcting phase were implemented to the procedure, professionals would have had to eliminate some of the proposed edges to obtain complete precision with 60%. When this method is included in the procedure, the coming graph model would indeed be completely reliable compared to that of a health knowledge graph developed by Google making it an experiential model for the physical world.

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