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Using network properties to evaluate targeted immunization algorithms

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Abstract
Immunization of complex network with minimal or limited budget is a challenging issue for research community. In spite of much literature in network immunization, no comprehensive research has been conducted for evaluation and comparison of immunization algorithms. In this paper, we propose an evaluation framework for immunization algorithms regarding available amount of vaccination resources, goal of immunization program, and time complexity. The evaluation framework is designed based on network topological metrics which is extensible to all epidemic spreading model. Exploiting evaluation framework on well-known targeted immunization algorithms shows that in general, immunization based on PageRank centrality outperforms other targeting strategies in various types of networks, whereas, closeness and eigenvector centrality exhibit the worst case performance.

Keywords targeted immunization; epidemic spreading; network properties; centrality measures; complex networks.

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1 Introduction

The threat of global epidemic spreading has resulted in widespread investigations on how to predict and control epidemics through populations (Gallos et al., 2007; Hadidjojo and Cheong, 2011; Hartvigsen et al., 2007; Salathé and Jones, 2010; Schneider et al., 2012, 2011). Vaccination is one of the most effective solutions which not only protects vaccinated people, but also can prevent transmitting disease among their friends (Cornforth et al., 2011). The traditional vaccination strategy, mass vaccination, might not always be feasible due to its high cost or scarce vaccination resources (Gallos et al., 2007; Hartvigsen et al., 2007; Vidondo et al., 2012). That’s the reason why targeted immunization strategies are of the current interest in public health area (Bishop and Shames, 2011; Chen et al., 2008; Cohen et al., 2003; Cornforth et al., 2011; Dezső and Barabási, 2002; Eames et al., 2009; Gallos et al., 2007; Gao et al., 2011, 2010; Hadidjojo and Cheong, 2011; Hartvigsen et al., 2007; Hébert-Dufresne et al., 2013; Masuda, 2009; Miller and Hyman, 2007; Niu et al., 2009; Peng et al., 2010; Restrepo et al., 2006; Salathé and Jones, 2010; Schneider et al., 2012, 2011; Vidondo et al., 2012; Yamada and Yoshida, 2012; Yoshida and Yamada, 2012). Targeted immunization strategies vaccinate intercommunal individuals whose immunization prevent infectious propagation among different communities (Masuda, 2009; Salathé and Jones, 2010).

Impact of close contacts on disease transmission has led to new studies on infectious propagation using social network analysis (Cornforth et al., 2011; Gallos et al., 2007; Hartvigsen et al., 2007; Salathé and Jones, 2010; Weerasinghe, 2013). In these investigations, relations are modeled as an undirected graph whose nodes represent individuals and links represent their relationships (Salathé and Jones, 2010). Node centrality is one of the most studied concepts in social network analysis which determines nodes influence on network flows (Borgatti, 2005; Christley et al., 2005; Freeman, 1978). Accordingly, Applying node centrality measures into targeted immunization have resulted in high performance of vaccination strategies (Chen et al., 2008; Cohen et al., 2003; Dezső and Barabási, 2002; Eames et al., 2009; Gao et al., 2011; Hébert-Dufresne et al., 2013; Masuda, 2009; Miller and Hyman, 2007; Niu et al., 2009; Restrepo et al., 2006; Salathé and Jones, 2010; Schneider et al., 2012, 2011; Vidondo et al., 2012). Several centrality measures have been used in targeted immunizations. Vaccinating highest degree node is the most common strategy (Chen et al., 2008; Cohen et al., 2003; Dezső and Barabási, 2002; Eames et al., 2009; Gallos et al., 2007; Gao et al., 2011, 2010; Miller and Hyman, 2007; Niu et al., 2009; Schneider et al., 2012; Vidondo et al., 2012), whereas, immunizing nodes with highest betweenness centrality is acknowledged as most effective targeted immunization (Chen et al., 2008; Hébert-Dufresne et al., 2013; Salathé and Jones, 2010; Schneider et al., 2012, 2011). Moreover, the relationship between largest eigenvalue of network adjacency matrix and epidemic threshold (Chakrabarti and Faloutsos, 2003; Chakrabarti et al., 2008; Peng et al., 2010) inspired many researchers to use other centrality measures such as eigenvector (Bonacich, 1987; Restrepo et al., 2006) and PageRank (Miller and Hyman, 2007; Page et al., 1999).

Several investigations have been carried out to assess ability of centrality measures in identification of influential spreaders or high risk individuals (see Table 1). In spite of implicit relevance between these problems and network immunization, they are inherently different (Zhang, 2012a, 2012b). Influential spreaders are nodes that lead to faster and wider spreading in complex networks (Chen et al., 2011; Kiss and Bichler, 2008). The high-risk individuals are people with high probability of being infected (Christley et al., 2005). In contrast, targeted node for immunization are nodes whose removal results in the maximum reduction of epidemic spreading in a network (Habiba et al., 2010). As seen in Table 1, the only known research about impact of centrality measures in targeted immunization is conducted by Habiba who compared centrality measures efficiency in identifying spread blockers based on simulation of independent cascade model (Habiba et al., 2010). Regarding this experiments, local centrality measures such as degree are good indicators of blockers. Unfortunately, this research only considered independent cascade model which is not reliable on other epidemic spreading models such as SIR. Additionally, the simulation of epidemic model requires high computational cost (Ventresca and Aleman, 2013).

In spite of many literatures in targeted immunization algorithm, a comprehensive analysis on performance of immunization algorithms has never been reported to our knowledge (See Table 2). Although several experiments have been conducted in order to evaluate immunization algorithms, they have significant shortcomings. First, a small number of efficient immunization algorithms are included (Holme et al., 2002; Schneider et al., 2012, 2011). Second, the experiments are conducted based on a single network (Eames et al., 2009; Miller and Hyman, 2007; Ventresca and Aleman, 2013) or network structure (Hartvigsen et al., 2007). Third, limited number of structural properties are considered (Holme et al., 2002; Masuda, 2009; Schneider et al., 2012; Ventresca and Aleman, 2013). Fourth, the goal of immunization algorithms is not discussed. Fifth, the time complexity of the immunization algorithms is mostly ignored. Finally, above all, only simulation of special epidemic model has been considered which is not extensible to other epidemics.

Table 1 Centrality measures evaluation in the literatures of epidemic spreading.

Purpose	Authors	Centrality measures	Best measure	Approaches
influential spreader	Kiss and Bichler, 2008	In/out Degree, Betweenness, Closeness, PageRank, SenderRank	SenderRank Out Degree	Measuring number of reached customers in marketing message spreading initiated by each measures
	Chen et al., 2011	Degree, Closeness, Betweenness	Closeness	Measuring the number of infected nodes at different time in SIR simulation initiated by each measure
high-risk individuals	Christley et al., 2005	Degree, Closeness, Betweenness, Random Betweenness	Degree	Exploring the relation between node centralities and risk of infection in SIR simulation
Spread blockers	Habiba et al., 2010	Degree, Closeness, Betweenness, PageRank, Clustering Coefficient	Degree	Measuring reduction in number of infected individuals in simulation of independent cascade model spreading

The contributions of this paper are as follows:

- We propose a new evaluation framework regarding amount of available vaccination resources, goal of immunization program and time complexity. Considering available amount of immunization resources, we assess immunization algorithms in case of limited and flexible amount of resources. Largest eigenvalue of network adjacency matrix, size of the largest connected component, and, sum of square partitions. Additionally, immunization threshold and network robustness are measures of evaluating immunization algorithms in case of unlimited or flexible amount of vaccination resources. The measures evaluate immunization algorithms regarding different goal of immunization program which is discussed later.

- We exploit the introduced evaluation framework to study the impact of well-known centrality measures (i.e. degree, betweenness, closeness, eigenvector, and PageRank) on targeted immunization algorithms in various real and artificial networks. Then, we suggest the most preferred immunization algorithms with regard to the network structure.

This paper is organized as follows: In section 2, we introduce our evaluation framework for evaluating the efficiency of immunization algorithms in case of limited amount of vaccination resources. Then, we review network centrality measures and investigate their relationship to epidemic spreading in section 3. Then, in section 4, our simulation setting and numeric result of applying is described. Finally, we conclude the whole paper in section 5.

Table 2 Evaluation of targeted immunization algorithms in literatures.

Literatures	Immunization algorithms	Networks		Efficiency Measures	
		Real	Model	Structural	Epidemic parameter [b]
Holme et al., 2002	Betweenness, Degree	HEP Computer network	Small-world, Scale-free, Erdös-Renyi	LCC [a], Distance	×
Miller and Hyman, 2007	Degree, PageRank	Episims	×	×	SIR T=1; $0<\alpha<1$
Hartvigsen,et al., 2007	Degree, Clustering coefficient	×	Small-world	×	SIR Simulation of Influenza R_0=2 T=3
Chen et al, 2008	Degree, Betweenness	HEP AS Workplace AS Metabolic	Scale-Free, Random-regular, Erdös-Renyi	Immunization threshold , LCC	SIR Simulation α= 0.2 β=0.05
Masuda, 2009	Degree, Eigenvector	HEP PGP WWW email-based	Erdös-Renyi	LCC	×
Eames et al., 2009	Degree, Weight, Secondary case	networks generated based on a conducted survey	×	×	SIR Simulation With different parameters
Schneider et al., 2012	Degree, Betweenness	HEP AS	Scale-free, Erdös-Renyi, Random-regular	LCC, Robustness	×
Ventresca and Aleman, 2013	Degree, PageRank, Total weight	Toronto social networks based on 2006 census data	×	LCC, Degree distribution, Clustering coefficient	×

[a] LCC: Largest connected component of network.
[b] Epidemic parameters (α: infectious rate, β: recovery rate , R_0: reproduction number, T= infectivity Time).

2 Evaluation Framework

To study impact of centrality measures in targeted immunization algorithms, we propose a framework to assess their efficiency in case of limited or flexible amount of vaccination resources regarding different goal of immunization program and time complexity (see Fig. 1). To evaluate immunization algorithms in limited amount of vaccination resources, the framework estimates expected epidemic growth in different situations. To assess their efficiency in case of flexible amount of vaccination resources, it captures their overall efficiency in case of unknown amount of vaccination resource in addition to their ability to minimize total cost of immunization. In the following, we describe this evaluation framework in details.

In case of limited vaccination resources, an immunization algorithm targets and vaccinates appropriate limited set of nodes whose immunization minimize the expected growth of epidemics. In this section, we talk about how to evaluate efficiency of immunized sets by targeted immunization algorithms

Recent investigation showed a strong relationship between epidemic spreading parameters and network structural properties(Ames et al., 2011; Aspnes et al., 2006; Chakrabarti and Faloutsos, 2003; Chakrabarti et al., 2008; Chen et al., 2008; Schneider et al., 2012, 2011; Ventresca and Aleman, 2013). Most important of structural properties are largest eigenvalue of network adjacency matrix, largest connected component of network, and, sum of square partitions. Details of our metrics are elaborated in the following.

2.1 Limited amount of vaccination resources

2.1.1 Increment of network epidemic threshold

Epidemic threshold is a parameter which determines whether an infection dies out over time or becomes an epidemic (Chakrabarti and Faloutsos, 2003; Chakrabarti et al., 2008; Kitchovitch and Liò, 2011; Masuda, 2009; Peng et al., 2010; Restrepo et al., 2006). Epidemic threshold of network is equal to inverse largest eigenvalue of network adjacency matrix (λ) (Chakrabarti and Faloutsos, 2003; Chakrabarti et al., 2008). Thus, an efficient immunization algorithm should reduce λ in order to reduce risk of outbreak contagious (Chakrabarti and Faloutsos, 2003; Chakrabarti et al., 2008; Masuda, 2009; Restrepo et al., 2006). To assess their ability to aim this, we measure the reduction of largest eigenvalue by calculating $E = \frac{\acute{\lambda}}{\lambda}$ where λ is the largest eigenvalue of the initial network and $\acute{\lambda}$ is the largest eigenvalue of the immunized network. Formulation of this problem is shown in Table 3.

Table 3 Formulation of immunization program with goal of increasing epidemic threshold in case of limited amount of vaccination resources.

Input	Social network (G),number of immunization resources (k)	G, k
Output	Subset of k nodes	S ⊆ V(G) such that ||S||=k
Goal	Reducing largest eigenvalue of matrix	Minimize λ(G/S)[a]

[a]λ(G/S) is largest eigenvalue of residual network after removal of S.

2.1.2 Reduction of worst expected epidemic size

A network connected component is defined as the set of all nodes which all are reachable from each other. Therefore, an infection that starts in a component cannot propagate to other components. Accordingly, in case of single source of infection, the worst case epidemic size is equal to size of largest connected component of network (LCC)(Chen et al., 2008; Gallos et al., 2007; Hadidjojo and Cheong, 2011; Masuda, 2009; Niu et al., 2009; Restrepo et al., 2006; Schneider et al., 2012, 2011; Ventresca and Aleman, 2013; Yamada and Yoshida, 2012; Yoshida and Yamada, 2012). Hence, the fraction of largest connected component of network is another important factor to assess efficiency of immunization algorithms. The formulation of this problem is shown in Table 4.

Table 4 Formulation of immunization problem with goal of minimizing worst expected epidemic size in case of limited amount of vaccination resources.

Input	Social network (G),number of immunization resources (k)	G, k
Output	Subset of k nodes	S ⊆ V(G) such that ‖S‖=k
Goal	Reducing largest connected component(LCC)	Minimize LCC(G/S)[a]

[a]LCC(G/S) is largest connected component of residual network after removal of S.

2.1.3 Reduction of mean expected epidemic size

In addition to worst case epidemic size, we estimate expected mean number of infected persons; if all individuals have equal probability to be initially infected, the probability of outbreak occurring in *ith* component is obtained by $(c_i/N)$where c_i is size of the component and *N* is network size. Therefore, the expected mean number of infected person (i.e. mean epidemic size) is $(\sum |c_i|^2/N)$ called sum of square partition (Aspnes et al., 2006). The formulation of this problem is shown in Table 5.

Table 5 Formulation of immunization problem with goal of minimizing mean expected epidemic size in case of limited amount of vaccination resources

Input	Social network (G),number of immunization resources (k)	G, k
Output	Subset of k nodes	S ⊆ V(G) such that ‖S‖=k
Goal	Reducing sum of square partition	Minimize SSP(G/S)[a]

[a]SSP(G/S) is largest connected component of residual network after removal of S.

2.2 Flexible amount of vaccination resources

To compare efficiency of immunization algorithms in case of flexible amount of vaccination resources, two metrics are provided: "immunization threshold" and "robustness". Immunization threshold and Robustness are numeric measures capturing overall efficiency of immunization algorithms where different amount of vaccination resources are available. We consider these measures on artificial networks with different size and degree.

2.2.1 Reduction of whole immunization cost

If sufficient amount of vaccination is available, an efficient immunization algorithm should minimize immunization cost of whole population. In other word, Immunization algorithm should suppress epidemics in very small component by removing minimal number of nodes (i.e. immunization cost). This ability of immunization algorithms is evaluated by their immunization threshold (q_c) which is the fraction of removal nodes when size of largest connected component is zero (Chen et al., 2008). The formulation of this problem is shown in Table 6.

Table 6 formulation of immunization problem with goal of minimizing immunization cost.

Input	Social network (G)	G
Output	A subset of nodes whose removal eradicate epidemic spreading	S ⊆ V(G) such that LCC(G/S)=0
Goal	Minimize number of immunization resource	Minimize ||s||

2.2.2 Reduction of worst case epidemic size in case of unknown amount of vaccination resources

If the supply of immunization doses is not known, an immunization algorithm is required which prioritize nodes such that average growth of epidemic during the whole immunization process is minimized (Schneider et al., 2012). Formulation of this problem is shown in Table 7.

Table 7 formulation of immunization problem with goal of minimizing worst case epidemic in case of unknown amount of vaccination resources.

Input	Social Network (G)	G
Output	An ordering of node (O)	O={$< o_1, o_2,\ldots,o_n >$}
Goal	Minimizing epidemic spreading in different amount of vaccination resources	Minimize R$= \frac{1}{n}\sum_{i=1}^{n} LCC\ (G/ (o_{1:i}))$

To measure efficiency of nodes ranking, Robustness (*R*), is defined by (Schneider et al., 2011) to capture overal efficiency of algorithm in case of unknown amount of vaccination resouces. This metric is calculated by Eq.(1) where *L(Q)* is the fraction of largest component of network when the fraction of immunized nodes is equal to *Q*.

$$R = 1/N\ (\sum_{Q=1}^{N} L(Q)) \quad (1)$$

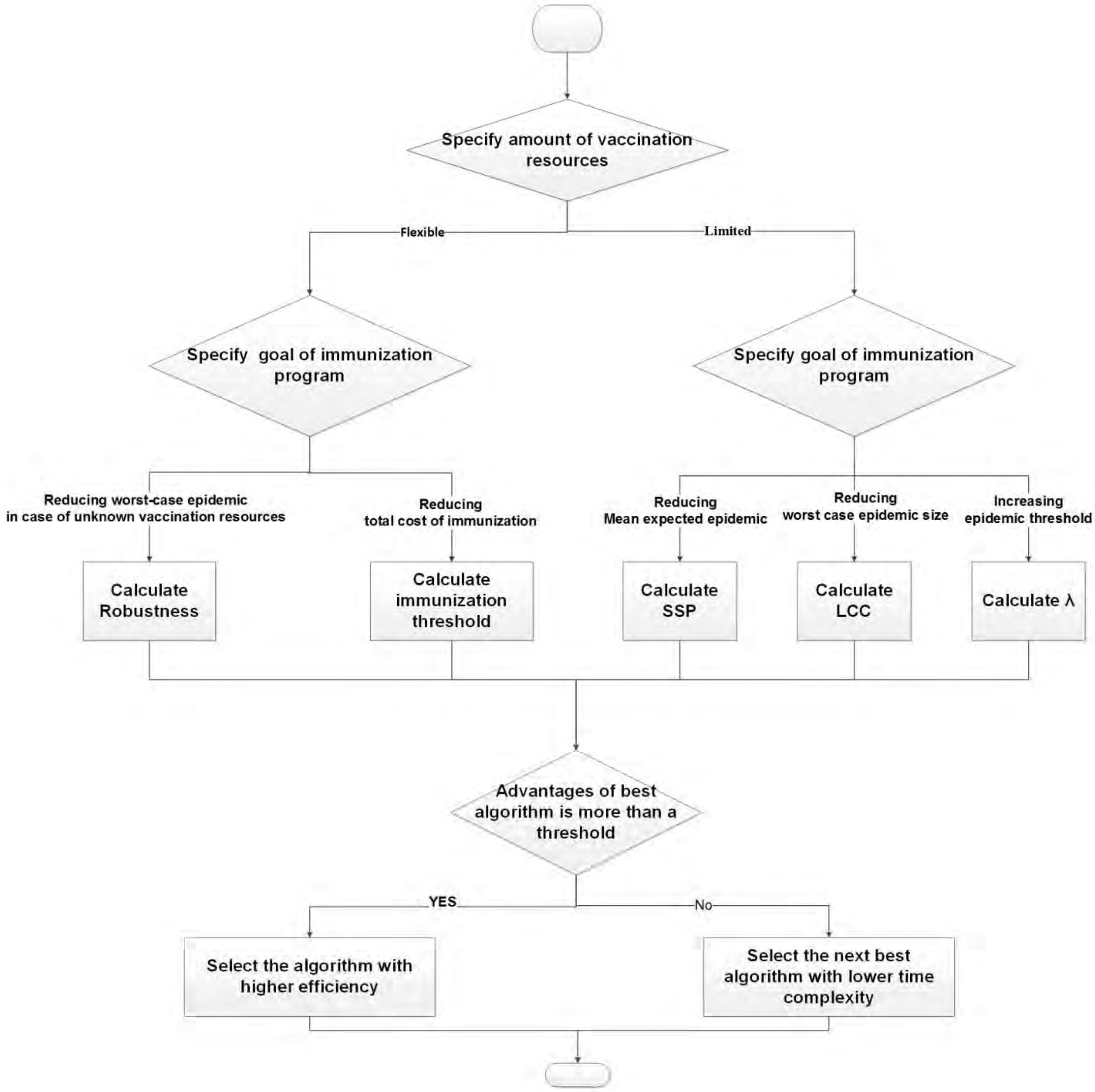

Fig. 1 Evaluation framework for immunization algorithms regarding amount of vaccination resource, goal of immunization program, and, time complexity.

3 Centrality Measures for Targeted Immunization

Regarding various aspects of nodes influence on epidemic spreading, different centrality measures are used in targeted immunization. In this paper, we study various centrality measures including degree, betweenness, closeness, eigenvalue and PageRank which are more applicable in epidemic spreading and targeted immunization (Chakrabarti et al., 2008; Chen et al., 2008; Christley et al., 2005; Cohen et al., 2003; Dezső and Barabási, 2002; Eames et al., 2009; Gao et al., 2011; Habiba et al., 2010; Hébert-Dufresne et al., 2013; Kiss and Bichler, 2008; Masuda, 2009; Miller and Hyman, 2007; Niu et al., 2009; Restrepo et al., 2006; Salathé and

Jones, 2010; Schneider et al., 2012, 2011; Ventresca and Aleman, 2013; Vidondo et al., 2012; Zhang, 2012a, 2012b).

To target and immunize nodes based on their centrality, two kinds of algorithms are generally proposed: initial and adaptive. Initial algorithms calculate node centrality in original networks and immunize *k* most *k* central nodes where *k* is number of available vaccination resource. On the other hand, adaptive algorithms recalculate node centralities in a network of non-immunized nodes after immunizing the most central node. This procedure is iterated until *k* node is immunized (Masuda, 2009; Restrepo et al., 2006; Schneider et al., 2012, 2011). Since the time complexity of initial algorithms is *k* time less than adaptive algorithms, the former one is more applicable for real networks. In this paper, we only consider the initial type algorithms.

A social network is an undirected network represented by adjacency matrix denoted by A; $A_{ij} =1$ when node *i* and node j are adjacent, and $A_{ij} =0$ otherwise. In the following, we review these centrality measures and their relationship with epidemic spreading.

3.1 Degree centrality

Degree centrality which is defined as number of connected links to a node, estimates immediate impact of node infection (Borgatti, 2005). Immunizing highest degree nodes (HD) minimizes network density which is an influential factor in growth rate of epidemic diseases (Hadidjojo and Cheong, 2011). Furthermore, vaccinating high degree nodes is exceedingly effective in scale-free (Dezső and Barabási, 2002) and sparse (Hébert-Dufresne et al., 2013) networks which in high degree nodes play an important role to connect other nodes.

$$d(i) = \sum_{j=1}^{n} A_{ij} \qquad (2)$$

3.2 Betweenness centrality

Betweenness centrality of each node is the proportion of times it lies on the geodesic paths between other nodes (Christley et al., 2005; Freeman, 1978).The betweenness centrality of node *i* is given by

$$BC(i) = \sum_{u\neq v\neq w} (g_{j,k}^{i}/g_{j,k}) \qquad (3)$$

where $g_{j,k}$is the number of geodesic paths from *j* to *k*, and $g_{j,k}^{i}$is the number of these geodesics that pass through node *i*.

Since nodes with high betweenness centrality bridge network communities (Habiba et al., 2010; Salathé and Jones, 2010), their immunization fragments network to smaller parts. Hence, an epidemic starts in a component cannot infect nodes in other components. Additionally, betweenness centrality is an effective measure to identify high risk individuals as it calculates volume of flow passing through each node (Borgatti, 2005). That is the reason why highest betweenness immunization (HB) is supposed as most effective targeted immunization algorithms.

3.3 Closeness centrality

Closeness centrality of a node is calculated by inverse sum of shortest distances of the node from all other ones.

$$CC(i) = \sum_{j\in V/v} d_G(i,j) \qquad (4)$$

where $d_G(v, t)$ is the geodesic distance between v and t (Borgatti, 2005; Freeman, 1978). If all nodes have equal probability to initiate an infection, nodes with highest closeness centrality are more prone to get infected (Borgatti, 2005; Christley et al., 2005). Besides, their infection result in faster epidemic spreading through network (Borgatti, 2005) . Therefore, highest closeness immunization (HC)not only vaccinates high risk individuals, but also postpones epidemic spreading through networks.

3.4 Eigenvector centrality

Eigenvector centrality provides a model of nodal infectious risk according to the risk level of its neighbours (Borgatti, 2005). Let *E(i)* be the eigenvector centrality of node *i* and $\tau(i)$ set of its netighbours, then

$$E(i) = (1/\lambda)\sum_{j\in\tau(i)} E(j) = (1/\lambda)\sum_{j=1}^{N} A_{ij}E(j) \qquad (5)$$

This equation can be rewritten in vector form such as Eq.(6) where $E = \{E(1), E(2), \ldots, E(n)\}$ and λ is the largest eigenvalue of network adjacency matrix.

$$E = (1/\lambda)\ AE \qquad (6)$$

$$\lambda E = AE \qquad (7)$$

Therefore, eigenvector centralityis defined as the principal eigenvector of the adjacency matrix of network (Bonacich, 1987). Moreover, it determines impact of removing nodes on epidemic threshold increment (i.e. reduction of λ)(Masuda, 2009; Restrepo et al., 2006).Let Eq.(8) be the linearized eigenequation after removal of node *k*

$$(\lambda + \Delta\lambda)(E + \Delta E) = (A + \Delta A)\ (E + \Delta E) \qquad (8)$$

It has been provedby (Restrepo et al., 2006) that

$$I_k = -\,(\Delta\lambda/\lambda) \cong E_k^2 / \sum_{i=1}^{N} E_k^2 \qquad (9)$$

where I_k is impact of removing node *k*on epidemic threshold and $E_k\ is$ eigenvector centrality of node *k*. Accordingly, immunization of nodes with highest eigenvector (HE) centrality reduces risk of infection through the network.

3.5 PageRank centrality

PageRank centrality, introduced by Google for webpage ranking, determines probability of visiting a node in a random walk (Page et al., 1999). In term of epidemic spreading, nodes with high PageRank centrality are more likely to be infected or infect others along many paths (Miller and Hyman, 2007). Therefore, their immunization eliminates lots of disease transmission routes. Since nodes with high PageRank centrality have many neighbours with low degree, highest PageRank (HP) immunization vaccinate influential nodes whose immunization strongly protects their neighbours (Miller and Hyman, 2007).

4 Experiments and Results

Here, we study the impact of centrality measures in initial targeted immunization using proposed evaluation framework. The proposed framework has been applied to various artificial and real networks to compare efficiency of different targeted immunization algorithms. Table 8 illustrates details of our experiments. We used igraph (Csardi and Nepusz, 2006) package in R.2.15.1 to generate artificial networks, compute nodes centrality, and evaluation metrics.

Table 8 Evaluation framework parameter settings.

Immunization algorithm	Vaccination resource	Efficiency measures	Datasets
Highest degree immunization (HD) Highest betweenness immunization (HDB Highest closeness immunization (HC) Highest eigenvector immunization (HE Highest PageRank immunization (HP)	Limited	Largest eigenvalue of network adjacency matrix (λ) Largest connected component of network (LCC) Sum of square partitions (SSP)	Real (HEP, FBL, AS) Artificial(SF, ER, SW)
	Flexible	Immunization threshold (q_c) Robustness (R)	Artificial withsize=10^4 and varying degree Artificial with average degree of 4 and varying size (10^2, 10^3, 10^4, 10^5)

4.1 Limited amount of vaccination resources

In case of limited vaccination resources, we compare ability of immunization algorithms in reduction of epidemic growth in various real and artificial networks. To aim this, we calculate evaluation criteria including largest eigenvalue of network adjacency matrix, largest connected component of network, and, sum of square partition.In the following, we describe datasets and numeric result.

4.1.1 Datasets

In order to evaluate efficiency of targeted immunization algorithms in case of limited budget, various real and artificial network datasets are used. Our real networks includes HEP (Gehrke et al., 2003; Leskovec et al., 2005) , AS (Shavitt and Shir, 2005), and Facebook-like (FBL) (Opsahl and Panzarasa, 2009), networks which are commonly used in immunization literature(Chen et al., 2008; Gao et al., 2011; Hu and Tang, 2012; Masuda, 2009; Mirzasoleiman et al., 2012; Niu et al., 2009; Schneider et al., 2012, 2011). The artificial network datasets include scale-free (SF) (Cho et al., 2009; Chung and Lu, 2002; Goh et al., 2001), Erdös-Renyi (ER) (Erdos, P. and Renyi, 1959) and small-world (SW) (Watts and Strogatz, 1998) networks. The structural properties of these networks are shown in Table 9.

Real datasets includes HEP, AS, and FBL networks. The HEP network represents citation network of high-energy physics theory derived from e-print Arxiv. It contains 27,770 nodes representing published paper and 352,285 undirected links representing citation between two papers (Gehrke et al., 2003; Leskovec et al., 2005). AS networks containing 25,367 nodes and 75,004 edges captures information of the Internet network at autonomous systems on June 2012 (Shavitt and Shir, 2005). The FBL includes information of 13,838 messaging on an online community of 1,899 students at University of California, Irvine (Opsahl and Panzarasa, 2009).

In addition to the real network, we generate artificial networks of scale-free (SF), small-world (SW) and Erdös-Renyi (ER) models based on parameters mention in(Chen et al., 2008). The SF network is generated using the algorithm presented in (Cho et al., 2009; Chung and Lu, 2002; Goh et al., 2001) by the following settings: network size is 10,000, edge number is 20,000 and γ is 2.5. We construct SW network by

Watts-Strogatz algorithm (Watts and Strogatz, 1998) such that network size is 10,000, mean degree is 4 and switching probability is 0.01. Finally, "*G(n,m)*" implementation of Erdös-Renyi algorithm (Erdos, P. and Renyi, 1959) is used to generate ER network containing 10,000 nodes and 20,000 edges.

Table 9 Dataset properties.

Network	N[a]	M[b]	<d>[c]	Std(d) [d]	CC [e]	λ [f]
HEP	27,770	352,285	14.57	25.371	0.11	111.25
AS	25,367	75,004	5.91	48.03	0.01	103.35
FBL	1899	13,838	12.68	24.46	0.05	48.14
SF	10,000	20,000	4	4.40	0.001	9.90
ER	10,000	20,000	4	1.98	0.000	5.22
SW	10,000	20,000	4	0.27	0.46	4.08

[a] N : Number of vertices
[b] M : Number of edges
[c] <d>: Average degree
[d] Std(d): Standard deviation of degree
[e] CC: Clustering coefficient
[f] λ: Largest eigenvalue of network adjacency matrix

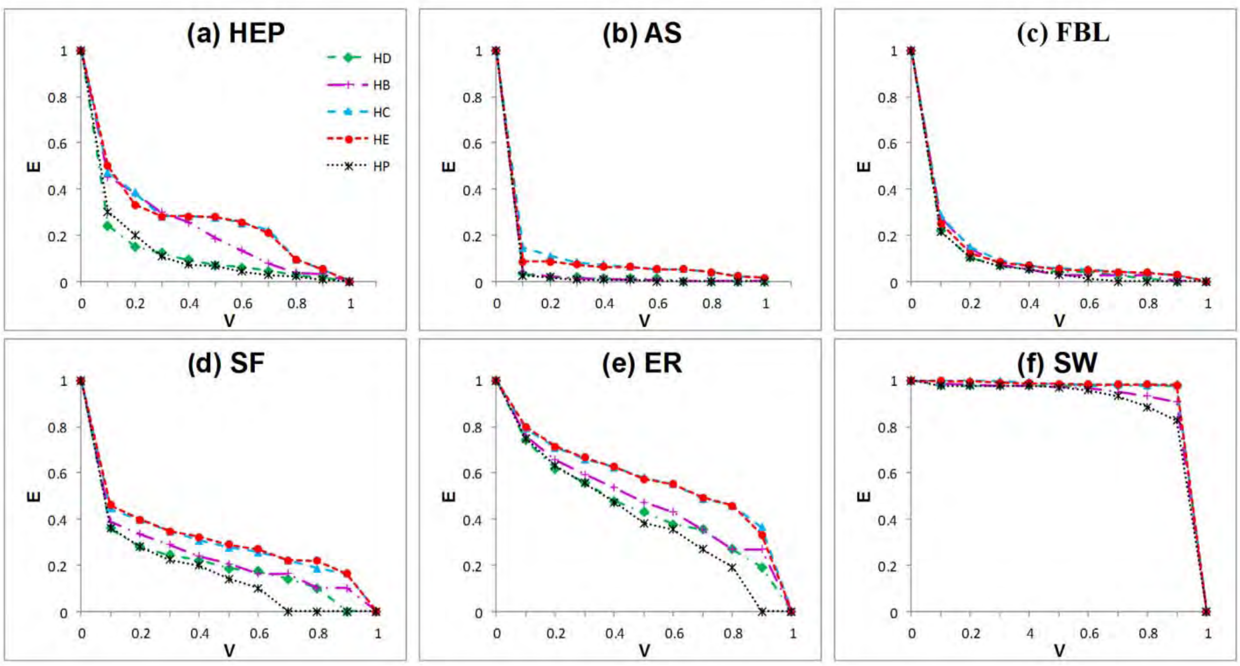

Fig. 2 The fraction of largest eigenvalue ($E=\hat{\lambda}\ /\ \lambda$) vs. fraction of immunized nodes (V). (a) HEP network. (b) AS network. (c) FBL network. (d) SF network. (e) ER network. (f) SW network.

4.1.2 Results

To assess their ability to decrease largest eigenvalue of network adjacency matrix, we calculated $E = \frac{\acute{\lambda}}{\lambda}$ where λ is the largest eigenvalue of the initial network and $\acute{\lambda}$ is the largest eigenvalue of the immunized network (Fig. 2). HP outperformed other strategies in all networks. HB and HD exhibited the next best performance in all networks. Their efficiency was very close to each other in all networks except HEP (Fig. 2a) where the initial largest eigenvalue is larger than other network (Table 9). Additionally, our experiments showed that as the largest eigenvalue of network decreases, the slope of *E* curves versus fraction of immunized nodes are also reduced (Fig. 2a, 2b, 2c). For instance, all algorithms required to immunize only 20% of FBL network to reduce *E* below 10%, while, they required to immunize more than 67% in order to reduce *E* to zero (Fig. 2c). This trend is also seen in HEP (Fig. 2a) and AS (Fig. 2b) networks. So we can conclude that there is a threshold below which λ decreases slowly. That could be the reason why targeted immunization did not perform well in artificial networks (Fig. 2d, 2e, 2f). In other words, their λ might be below the threshold.

Moreover**,** we evaluated efficiency of immunization algorithms in reducing worst-case epidemic size by plotting *L* versus *V* where *L* is fraction of largest connected component of network, and, *V* is fraction of vaccinated nodes (Fig. 3). HP, HD and HB took high advantages of reducing *L* in all networks. The performance of HD and HP were close in all network except SW which is more homogenous than other networks. In SW network, the efficiency of HD is reduced in case of immunization coverage more than 10% since the degree of 90% of nodes have equal degree.On the other hand, HB exhibited high performance in SW networks (Fig. 3f). The high efficiency of HB and HP in this network is explained by high clustering coefficient and low average distance properties of small-world networks (Watts and Strogatz, 1998) (Table 9). In the other word, there are few nodes with high PageRank and betweenness centrality lying on the paths between different clusters of networks. HC and HE performed weaker than other strategies in all network but their weakness is less in HEP (Fig. 3a) and FBL (Fig. 3c) networks which are denser than others (Table 9).

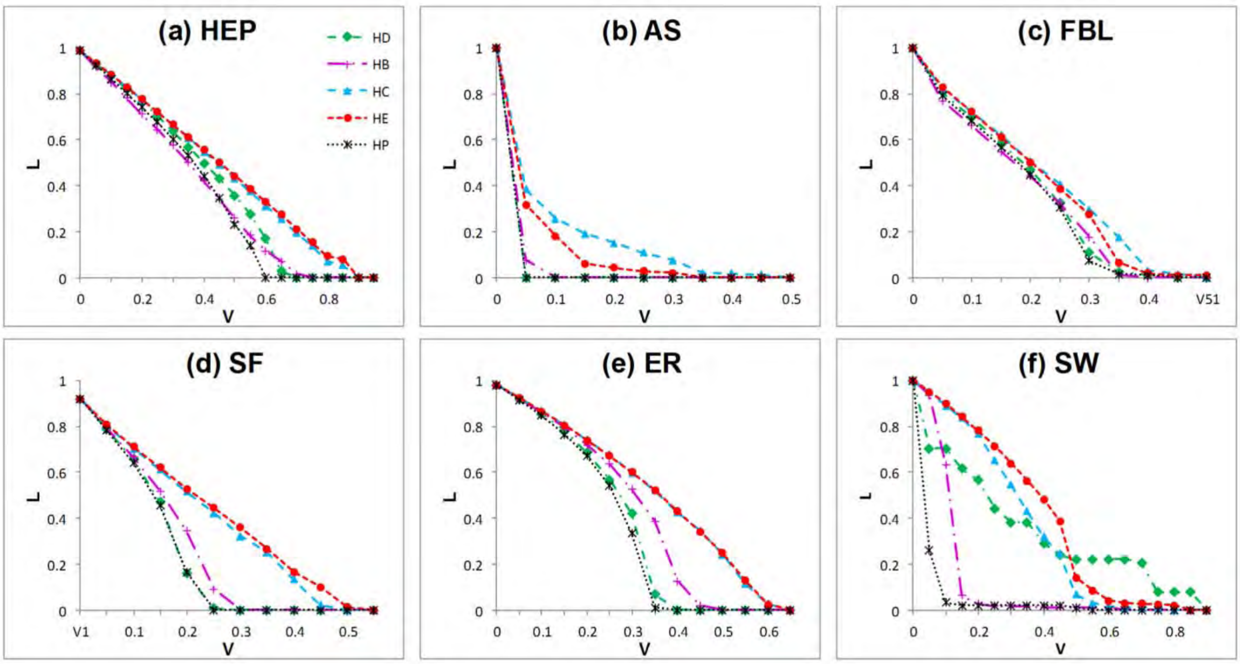

Fig. 3 Fraction of largest connected component (L) vs. fraction of vaccinated nodes (V). (a) HEP network. (b) AS network. (c) FBL network. (d) SF network. (e) ER network. (g) SW network.

In Fig. 4, we plotted *S*, the fraction of expected worst-case epidemic size (i.e. sum of square partitions), versus *V*, the fraction of vaccinated nodes in Fig. . It is obvious that changes of *S* are similar to the changes in worst case epidemic size (Fig. 4) but has a little shift to left. This is because of the fact that expected mean number of infected persons is proportional to sum of square of component size. In the other words, sum of square partitions highlights larger connected components in contrast to smaller ones more clearly. Therefore, the similar trends of *S* and *L* means all centrality measures failed to fragment networks to balanced partitions.
Regarding all criteria, HP exhibited the best performance, while, HE and HC exhibited the worst performance in all networks. HD and HB exhibited an acceptable performance in all networks. HD performed better in sparse and heterogeneous networks such as SF network, while, HB performed well in modular and homogenous networks such as SW network.

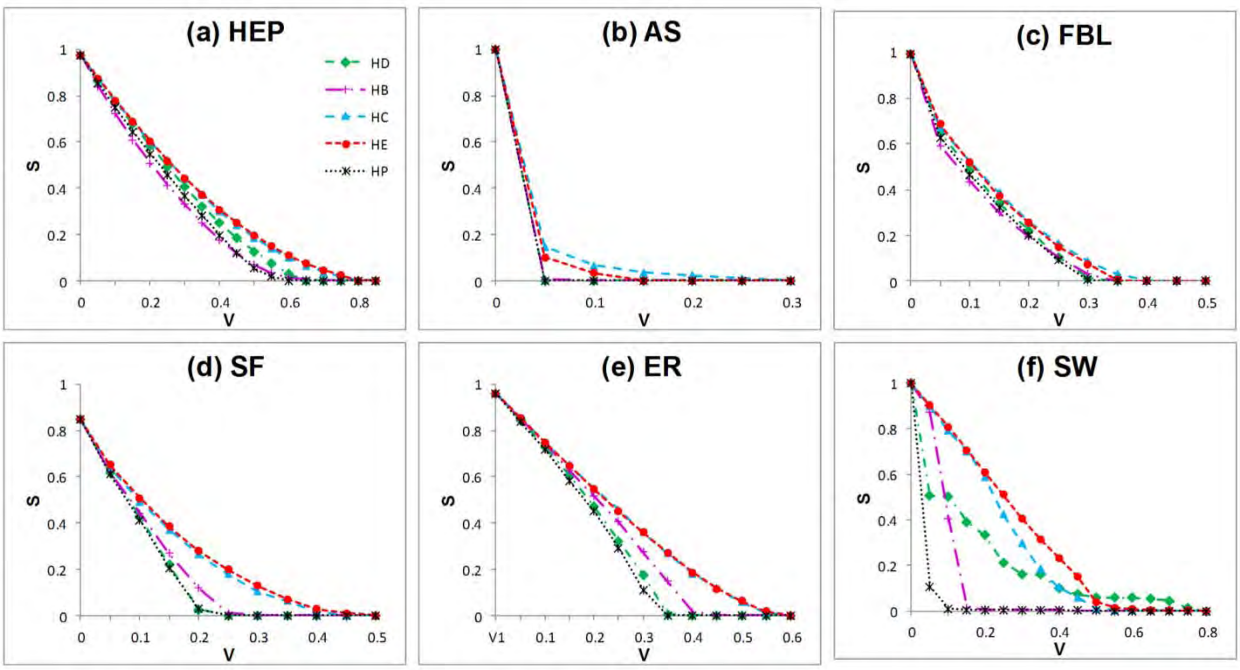

Fig. 4 Fraction of sum of square partitions (S) vs. fraction of vaccinated nodes (V). (a) HEP network. (b) AS network. (c) FBL network. (d) SF network. (e) ER network. (g) SW network.

4.2 Flexible amount of vaccination resources

We evaluate immunization algorithms in case of flexible amount of vaccination resources by computing their "immunization threshold" and "robustness" in artificial networks with different size and degree. The description of datasets and results are explained in the following.

4.2.1 Datasets

In order to assess efficiency of immunization algorithms in case of flexible amount of vaccination resources, artificial networks with different size and degree are generated. We generate scale-free, small-world, and, Erdös-Renyi networks with different size and degree. To compare efficiency of immunization algorithms in networks with different size, each type of artificial networks is generated with 100, 1000, 10,000, and, 100,000 nodes and average degree of 4. Additionally, artificial networks are generated in size of 10,000 and degrees up to 20 to evaluate immunization algorithms in networks with different density.

4.2.2 Results

To compare efficiency of centrality measures in minimizing immunization threshold (q_c), we plotted it as a function of network size (*N*) or average degree (<d>) for all artificial network models. Our experiments showed a directed relationship between network degree and q_c for all algorithms in majority of networks (Fig. 5). That is because of the weak connectivity in sparse networks in contrast to strong relations in dense network. In the other words, sparse networks can be fragmented to small component by removing only a few nodes, while, it is impossible to fragment dense networks.

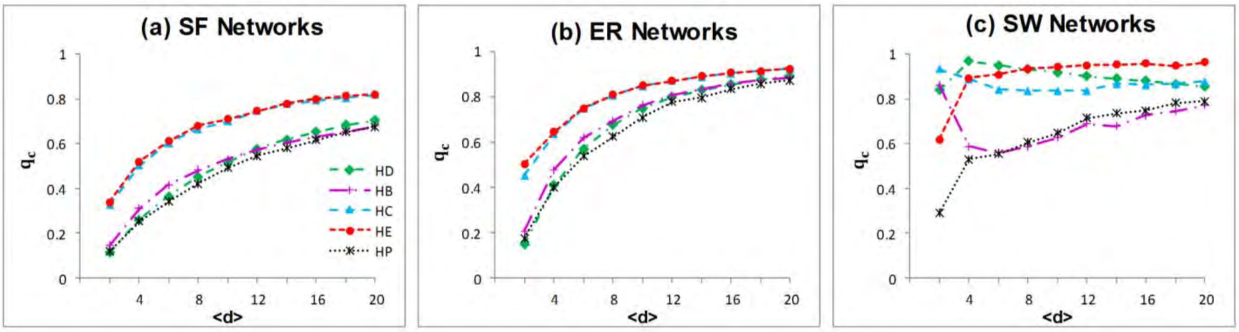

Fig. 5 Immunization threshold (q_c) vs. network average degree (<d>). (a). Scale-free networks (b) Small-world networks. (c) Erdös-Renyi networks. Average degree of all networks is 4. Each point is averaged on 10 different networks.

Considering immunization threshold of networks with different size, HP outperformed other strategies especially in small-world network (Fig.6c). For instance,q_c of HP in largest small-world network is 12% less than HB, 59% less than HC, 71% less than HE, and 85% more than HD. Despite of weak performance of HD in small-world networks, it performed well on scale-free and Erdös-Renyi networks (Fig. 6) such that the maximum difference between its immunization threshold and HP is about 7%. That is because of heterogeneous degree distribution in scale-free and Erdös-Renyi networks compared to homogenous degree distribution in all small-world networks.

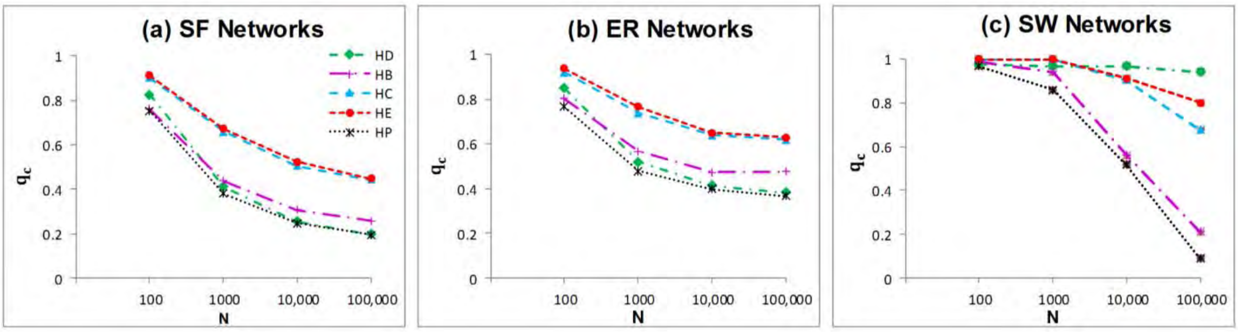

Fig. 6 Immunization threshold (q_c) vs. network size (N). (a). Scale-free networks (b) Small-world networks. (c) Erdös-Renyi networks. Average degree of all networks is 4. Each point is averaged on 10 different networks.

In addition to immunization threshold, we calculate network "robustness", R, of each algorithm. Our experiment showed that impact of degree increment on robustness is similar to its impact on immunization threshold in all networks (Fig. 7). It can be also explained by strong connectivity in dense networks which make it hard to fragment them.

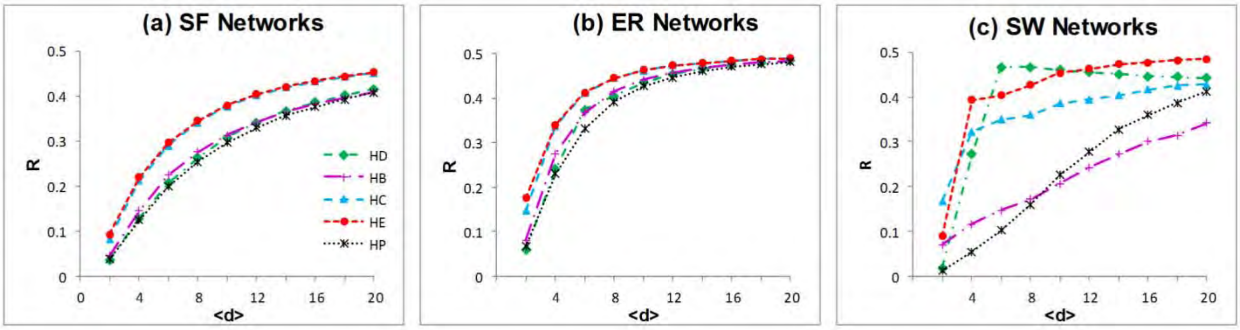

Fig. 7 Network Robustness (R) vs. network average degree (<d>). (a). Scale-free networks (b) Small-world networks. (c) Erdös-Renyi networks. All networks contain 10,000 nodes. Each point is averaged on 10 different networks.

Increasing the network size in scale-free networks reduced *R* about 10% to 14% (Fig. 8a), while, robustness of Erdös-Renyi networks fluctuated about 1% around a fixed value for all algorithms (Fig. 8b). This result is explained by random structure of Erdös-Renyi networks leading to emergence of a giant component which is hardly fragmented. On the other hand, efficiency of algorithms are much better in large scale-free networks compared to small ones with constant degree since central node plays an important role in connecting majority of nodes in large scale-free networks. Increasing small-world networks size had different impacts on robustness of algorithms; the robustness was reduced more than 22% for HP and HB, whereas, increased slightly for HE and HC when network size exceed 1,000 (Fig. 8c).

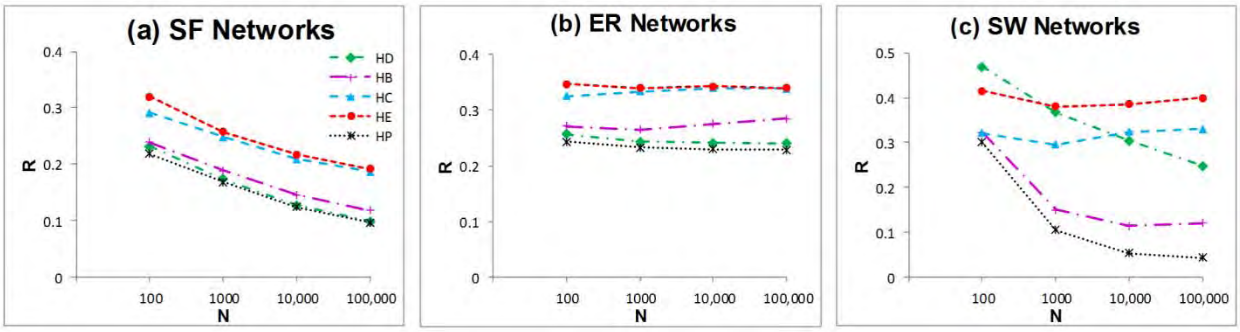

Fig. 8 Network Robustness (R) vs. network size (N). (a). Scale-free networks (b) Small-world networks. (c) Erdös-Renyi networks. Average degree of all networks is 4. Each point is averaged on 10 different networks.

5 Conclusion and Suggested Future Work

Due to high cost and limited resources of vaccination, there is a growing interest in targeted immunization strategies. Targeted immunization strategies vaccinate a subset of individuals whose vaccination minimize epidemic spreading through population. Regarding impact of contact networks on disease transmission, majority of immunization strategies use network centralities to prioritize nodes for vaccination.

In this paper, we first proposed an evaluation framework to study targeted immunization algorithms regarding amount of vaccination resources, goal of immunization program, and time complexity. The framework assesses efficiency of immunization algorithms in case of limited or flexible amount of vaccination resources based on network properties. The evaluation metrics for limited resources consist of the largest eigenvalue (i.e. immunization threshold), the largest connected component of network (i.e. worst case epidemic size), and, sum of square partitions (i.e. mean worst epidemic size. Metrics for flexible resources include immunization threshold (i.e. cost of complete immunization) and robustness (i.e. overall efficiency of immunization algorithms in case of unknown amount of vaccination resource).Next, we studied impact of five centrality measures including degree (HD), betweenness (HB), closeness (HC), eigenvector (HE) and PageRank (HP) in initial targeted immunizations based on the proposed evaluation framework.

In case of limited budget, HP exhibited the best performance, but, HC and HE exhibited the worst performance regarding all criteria. In heterogeneous networks such as AS and scale-free networks, efficiency of degree immunization was very close to PageRank immunization, whereas, it exhibited a weak performance in homogenous networks (e.g. small-world networks). Hence, degree immunization is more preferred in heterogeneous networks (e.g. AS and scale-free networks) due to its lower time complexity in comparison to PageRank immunization (Table 10). Closeness and eigenvector centralities were too weak in comparison to other algorithms in all networks. Additionally, comparing sum of square partitions and largest connected component of immunized network showed that all targeted immunization were unsuccessful to fragment network to balanced component. Furthermore, it should be noted that all immunization algorithms failed to reduce largest eigenvalue of artificial network adjacency matrix. Surprisingly, despite of relationship between eigenvector centrality and largest eigenvalue (Masuda, 2009; Restrepo et al., 2006), it did not show any advantages in comparison to other strategies. Therefore, these algorithms are not given preference in none of networks.

Table 10 Time complexity of node centrality calculation.

Centrality	Complexity [a]	Execution Time [b]					
		FB	AS	HEP	SF	SW	ER
Degree	O(N)	0	0.02	0.05	0	0	0
Betweenness	O(MN)	0.40	174.15	401.46	10.01	9.61	11.93
Closeness	O(MN)	0.77	58.98	170.31	5.65	5.08	6.70
Eigenvector	O(M+N) [c]	0	0.11	0.25	0.06	0.36	0.07
PageRank	O(M) [d]	0.02	0.27	0.74	0.07	0.06	0.06

[a] The Complexity times are based on implementation of igraph package where N is network size and M is number of edges.
[b] The execution times are measured in millisecond on a computer running an Intel core i7- i2670QM processor at 2.20Hz with 8GB of RAM.
[c] Depends on the input graph, usually it is O(|M|+|N|).
[d] Depends on the input graph, usually it is O(M).

In case of flexible amount of vaccination resources, we evaluated immunization threshold and robustness of algorithms in artificial networks with different degree and size. Considering both metrics, our experiments showed that PageRank outperforms other strategies in all networks except dense small-world network which in betweenness overtook it; nevertheless, betweenness immunization is still not an appropriate strategy for these networks due to its high time complexity. The best implementation of betweenness calculation of networks with N nodes and M edges goes as complexity of $O\ (MN)$ (Brandes, 2001) that converges to $O(N^3)$ for dense network which is far more than PageRank time complexity (Table 10). Therefore, PageRank immunization is strongly recommended for all networks especially in dense, homogenous, and clustered networks. Our recommendation for each model network considering time complexity and goal of immunization is given in Table 11.

Table 11 Recommended algorithm for artificial networks considering evaluation framework.

	Limited amount of vaccination resources			**Flexible amount of vaccination resources**	
Goal	Maximizing epidemic threshold (λ)	Minimizing worst-case epidemic (LCC)	Minimizing expected worst epidemic size (SSP)	Minimizing immunization cost (q_c)	Minimizing average growth of epidemic in case of unknown amount of resources (R)
Scale-Free	HP	HD	HD	HD	HD
Erdös-Renyi	HP	HP	HD	HP	HD
Small-World	HP	HP	HP	HP	HP [a]

[a] HB is more preferred than HP in small dense small-world network.

Although, these targeted immunization algorithms show high advantages of lowering cost in comparison to mass and random vaccination, their performance is still so far from an optimal solution especially in dense networks where strong connectivity makes it hard to fragment. Therefore, it is a new line of research to present immunization algorithms to optimize evaluation criteria. Additionally, it is necessary to study about the reasons why immunization algorithms failed to reduce largest eigenvalue of artificial network adjacency matrix. Furthermore, it is valuable for future research to evaluate targeted immunization in improving epidemic parameters (e.g. epidemic period and size) by simulating epidemics model (e.g. SIR, SIS, and SI) models. Finally, it is helpful to suggest the most preferred immunization algorithms with regard to network structure and epidemic spreading model

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