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Predictive triage for testing may improve control of a COVID-19 epidemic while reducing testing requirements

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Abstract

Background Extensive population testing played a crucial role in mitigating the COVID-19 pandemic. However, scaling up testing capacity requires a considerable workforce and infrastructure. Furthermore, sampling and testing delays can hinder timely interventions. We therefore sought to improve pre-test triage through an ensemble model based on self-reported information.

Methods We trained an XGBoost classifier to predict individual risk of COVID-19 infection for higher education students in Leuven (Belgium) from real-world social and health data related to 38,180 test results. The model could recommend isolation, testing, or release of individuals at high, moderate, or low risk of infection, respectively, based on two parametrizable probability thresholds. We then studied the epidemiological impact of the ensemble triage tool in silico, by simulating its implementation in our context to control an epidemic over time.

Results The predictive model achieved a ROC AUC of 77.5%, but its performance varied across rolling retraining windows. The epidemiological simulations highlight the potential of the ensemble-enhanced triage system to control a surge of infections in the student population of Leuven. Given a rapid implementation at the onset of an infection surge, it could reduce the effective reproduction number below 1.0 while reducing the testing requirements by 47%. The predictions of the ensemble model were strongly influenced by the number of contacts which individuals reported, the reason for testing, and the onset of symptoms.

Conclusions Our study suggests that pre-test triage guided by ensemble models could play an important role in allocating testing resources efficiently. Given timely implementation and isolation compliance within the population, it could also help rapidly control a surge of infections. Future research could validate this approach for other pathogens, in other settings, and with deep learning models.

Keywords Triage, COVID-19, Health policy, Ensemble methods, Machine learning, Decision support system

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Text box 1. Contributions to the literature

- This study presents a pre-diagnostic triage system that refers individuals at high, moderate, or low risk of infection to isolation, testing, or no intervention, respectively.
- The risk of infection is predicted by an ensemble model based on individual health and social data.
- The implementation of our triage system could have reduced the effective reproduction number for COVID-19 below 1.0 while saving tests in the student population in Leuven.
- Our triage system is parametrizable by public health experts and policy makers along the epidemic phases.

Background

During the coronavirus disease 2019 (COVID-19) pandemic, mitigation measures were implemented to control the number of infections within the population. Namely, lockdown measures were repeatedly implemented in many countries. While such measures allow rapid control of an epidemic, they are not sustainable and induce consequent economic and social impact on the society, especially on vulnerable groups [1]. Targeted measures, such as large-scale testing programs, were established to detect infected cases within the population and prevent onward transmission through isolation. Testing also enabled contact tracing and epidemiological data gathering. Despite inevitably missing infected cases within a population, test and trace systems could efficiently control outbreaks by decreasing the effective reproduction number [2, 3]. In this study, we refer to epidemic control as the implementation of public health and social measures in order to limit the propagation of a pathogen and therefore decrease its effective reproduction number. With such measures, the reduction in transmission is achieved with two basic mechanisms: reducing contacts and making contacts safer [4]. During surges of infection, test centers could become overloaded, and testing delays and turnaround times often increased, favoring further disease transmission [5].

Optimizing test and trace strategies requires addressing different aspects of the procedure, depending on the purpose of the measures implementation. For instance, for screening or surveillance, increasing testing frequency and reducing reporting delays tend to reduce the reproduction number [6]. The choice of the testing target group can also influence the testing efficacy. Grassly and colleagues have shown that prioritizing high-risk groups like symptomatic individuals and healthcare workers can reduce their contribution to pathogen transmission. The effectiveness of testing also strongly depends on the coverage [7]. When the number of tests is limited, a test allocation strategy can help maximize the number of positive cases detected in the population [8]. Also, shifting resources from hospital-based reactive testing to proactive community-based screening and prevention optimizes the control of COVID-19 [9]. A system of triage might help allocate the most informative tests only and might therefore reduce the required test capacity and mitigate delays issues.

During the COVID-19 pandemic, triage systems were implemented in several countries. These systems often aimed at patients in emergency departments (ED), or at predicting the evolution of the severity of a disease in intensive care units (ICU) [10, 11]. The key risk in such triage is underestimation of illness severity, resulting in increased mortality and morbidity [12]. Here, we investigate triage systems for diagnostic testing of mild infections. Such systems present a different type of risk: missing infected cases who may continue to spread the disease in a population. This risk increases when the prevalence of the disease rises [13]. Due to the different risks, these two categories of triage differed in their method of implementation. In ED or ICU triage systems, the decisional process was either based on a protocol, following national recommendations, or based on algorithms, such as a multivariate logistic regression method [14, 15]. The decision process typically required involvement of a healthcare professional, and was, in other instances, conducted through an online questionnaire [11, 16, 17]. Often, the triage decision was based on data gathered for individual cases, like symptoms, recent exposures, and travel history. Some hospitals also implemented triage after complementary investigation, such as an initial computed tomography (CT) scan or a blood analysis [10, 18–20]. Triage before polymerase chain reaction (PCR) testing often involved rapid testing, which allows to decrease high-accuracy diagnostic testing requirements [13].

Machine learning (ML) has widely been applied to predict the risk of COVID-19 infections during the pandemic. Both diagnostic and prognosis models were trained for practical application. While some prognosis models were used to predict COVID-19 related risk within the general population, many models were trained to predict outcomes of patients with diagnosis of COVID-19 [21]. Notably, Estiri and colleagues developed a ML framework capable of predicting individualized risks of hospitalization, ICU admission, need for mechanical ventilation, and death [22]. Although many studies used clinical data gathered by medical experts, Diaz Badial and colleagues trained models to predict the risk of COVID-19 infections solely based on self-reported data [23]. Predictive models were also embedded within triage systems. Notably, Liang and colleagues developed a web-based triage tool which integrated a deep neural network capable of predicting the risk of critical illness [24]. Wu and colleagues developed a decision support system to predict the severity risk at hospital admission based on logistic regression model. Their system

classifies the patient within low, medium, and high risk according to probability thresholds [25]. Kamran and colleagues also developed a triage system at hospital admission. They trained an ensemble of regularized logistic regression models to predict the risk of clinical deterioration. They adapted the threshold for low-risk patients based on the negative predictive value which they tolerated [26]. In this study, we define predictive triage as a decision system that uses supervised learning classifiers to stratify individuals by their risk of infection and, based on this risk, recommends different public health and social interventions [27].

The COVID-19 pandemic was characterized by a succession of waves of infections, often closely related to the evolution of the different variants of concern. We indeed observed a repeated succession of epidemic phases: (i) periods with stable incidence, typically observed between waves of infections, (ii) surges of infections, and (iii) periods during which the incidence decreases, usually after the population has acquired an immunity or following the implementation of strict control measures [28]. Moreover, the different variants of concern were characterized by different transmission dynamics and epidemiological parameters (evolving incubation period, serial interval, reproduction number) [29, 30]. The rapid evolution of the COVID-19 incidence and of the transmission characteristics of these variants offered challenges for the rapid adaptation of public health and social measures [28]. Similar patterns in the incidence of a disease are also observed for seasonal respiratory pathogens like influenza and respiratory syncytial virus (RSV) [31].

Despite the development of various predictive applications and their use within triage tools, to our knowledge no study proposed a methodology to develop a parametrizable ML-integrated triage tool, with a simulated epidemic impact of the implemented triage strategy. Also, many studies aim to predict the clinical evolution of a patient, after a positive test. In this study, we aimed to predict the risk of COVID-19 infection before any medical diagnosis, among university students in Leuven from November 2020 to May 2022. In other words, unlike many studies which aimed to perform triage at hospital level, we aimed to develop a triage methodology at community level, solely based on self-reported data. Finally, this ensemble-enhanced triage system must be agile, i.e., adapt to the different phases of an epidemic and to the evolution of transmission parameters. We also aimed to model the impact of triage both on the number of tests performed and on the effective reproduction number.

Methods

Data collection

During the COVID-19 pandemic, a dedicated test center was established to detect COVID-19 cases in the university student population of Leuven (Belgium). The test center remained active from September 2020 until May 2022, providing PCR tests on nasopharyngeal samples [2]. Before sample collection, students could report individual information via online forms, and via a face-to-face interviews with the workers at the test center. For each PCR outcome, our dataset includes all individual data reported before sample collection, together with contextual information recorded on the sampling date.

The individual information refers to health and social data reported by the students. Health data includes the symptoms onset date if any, the vaccination date if any, the date of the latest positive PCR outcome if any, and the reason for testing. Social data represent both the past social interactions of the students, and information about their place of residence. Notably, students reported recent contacts, whether they knew their possible infection source person, in which context and when they interacted, and whether they attended a possible super-spreading social gathering. Students also reported any countries in which they traveled recently, and the travel date. Social data also includes whether the individual lived in a student residence, whether they shared cooking or sanitary facilities, with how many other persons, and whether another individual recently tested positive for COVID-19 in their residence (Supplementary Fig. A1).

In addition, we included contextual variables representative of the epidemic (incidence history, positivity rate history, stringency index history) and the recent history of the environmental situation (precipitations, temperature, humidity, pressure) on the sampling date (Supplementary Table A1). From those self-reported and contextual data, we developed a pre-test ML-based triage strategy, which predicts the individual risk of COVID-19 infection. In this study, we investigate how self-reported data in a student population can be used to help predict their risk of infection, and further refine individual-targeted test-trace-isolate measures within the same population.

Predicting the risk of infection with machine learning

We preprocessed the data set by removing unrealistic outliers. Namely, we excluded individuals with unrealistic data, such as inconsistent symptom onset dates, inconsistent travel dates, or who reported sharing a household with ten thousands individuals. We assumed that such values reflected erroneous data. We also excluded students who received a PCR test, but who did not fill out any pre-test questionnaire. Within the dataset, we included the main reason for individuals to require a PCR test as a predictor. Among others, the reason for testing could be their willingness to confirm a positive COVID-19 rapid lateral flow test with a PCR test. We excluded all individuals who reported this reason, since

the high accuracy of antigenic self-tests could bias the machine learning model towards positive predictions and therefore bias the evaluation of the performance of the machine learning model [32]. We then standardized numerical data (mean of 0 and standard deviation (SD) of 1) and transformed categorical data using one-hot encoding. This method resulted in a data set of 38,180 PCR test results with relevant individual information (Supplementary Fig. A2). Supplementary Fig. A3 illustrates the patterns of missing and available values in the dataset.

Ensemble techniques were used to train the predictive model, as those algorithms demonstrated high performance in predicting individual infection risk from structured datasets [33]. We first validated the algorithm used in this study, and its corresponding optimal hyperparameters with a nested cross-validation algorithm [34]. We then evaluated the evolution of the performance of the machine learning models with those parameters. We simulated chronological training of the ensemble model based on the most recently collected data and evaluated it weekly. We defined four-week periods which we shifted by one week over the whole period. We trained the ensemble model based on the data collected during the first three weeks and tested it on the dataset collected during the fourth week. We imputed missing values for each window with the mean and the mode of available numerical and categorical variables respectively [35]. We evaluated the variable dependencies with Bayesian networks and we evaluated the influence of the variables on the ensemble model with Shapley values [36].

Test allocation for epidemic control

The predictive model aims to isolate, test or release students individually, respectively at high, moderate, and low risk of infection. This triage strategy is defined by two thresholds for the infection risk: the isolation threshold, above which we advise the student to isolate, and the release threshold, below which we release the student without any intervention. The thresholds are configured based on two parametrizable metrics:

- Release false negative rate ($FNR_{release}$): the proportion of COVID-19-positive patients we allow the model to release without undergoing testing (missed cases).
- Isolation false positive rate ($FPR_{isolation}$): the proportion of COVID-19-negative persons we allow the model to isolate without undergoing testing.

Over the course of an epidemic, incidence may vary considerably in a series of epidemic waves, due to seasonality or emergence of new variants. The two parametrizable metrics $FNR_{release}$ and $FPR_{isolation}$ must therefore be rapidly adaptable according to the epidemic situation. In general, a low $FNR_{release}$ means that few COVID-19-positive cases are released, i.e. most COVID-19-positive patients are detected and either tested or isolated. Thus, a low value of this parameter ensures a strong epidemic impact. However, increasing this parameter increases the tolerance of the triage system and alleviates the pressure on the test center. The second metric, $FPR_{isolation}$, has a direct impact on the societal compliance to use the triage system. Indeed, increasing this parameter increases the proportion of the individuals advised for direct isolation, which alleviates the pressure at the test center. However, a high $FPR_{isolation}$ reflects a high proportion of COVID-19-negative individuals advised for isolation. Thus, a high value may decrease the trust of individuals in the decision of the triage system. The choice of those two parameters must therefore represent a compromise between test capacity, epidemic control, and public trust.

We illustrated the use of the triage system by simulating its effect on testing requirements while controlling the epidemic. We defined three triage measures adapted to different epidemic phases (stable incidence, surges of infections, decreasing incidence), and configured them with fixed $FNR_{release}$ and $FPR_{isolation}$ values (Table 1). The start date of each epidemic phase was determined by observing the evolution of the incidence over the previous two weeks:

Table 1 Hypothetical triage metrics to simulate control of the epidemic across various phases. The first triage measure aims to only test individuals at risk of infection. When the incidence remains stable over time, the triage system is configured to not isolate any individual and to release 80% of the COVID-19-positive cases. When the incidence increases or when we observe a surge of infections, isolation policies must be more strict. This phase is associated with a high demand for testing. The triage system is configured to isolate 25% of COVID-19-negative individuals the most at risk and to only release 10% of COVID-19-positive cases. When the incidence decreases, isolation measures can be relaxed. We configured the ensemble triage to only isolate 10% of COVID-19-negative individuals and to release 35% of COVID-19-positive cases. The configuration of the two parameters was motivated by estimating the impact of each triage measure on R_e

Epidemic context (past two weeks)	Triage goal	$FPR_{isolation}$	$FNR_{release}$
Stable incidence	Referral for testing	0.00	0.80
Increasing incidence/Surge of infections	Rapid isolation of high risk and testing of intermediate risk	0.25	0.10
Decreasing incidence	Rapid isolation of very high risk and testing of high risk	0.10	0.35

- Referral for testing: Between the epidemic waves, no strong epidemic control is required. Only individuals at high risk of infection are advised for testing.
- Rapid isolation of high risk and testing of intermediate risk: During surges of infections, control measures must be more strict. Most individuals must therefore be tested or directly isolated. Only few individuals at low risk of infection are released.
- Rapid isolation of very high risk and testing of high risk: When the incidence decreases, the control measures can be alleviated. Immediate isolation is only advised for individuals at very high risk of infection, and testing is only advised for individuals at high risk of infection. This configuration is suitable for periods of decreasing incidence.

The two metrics are derived from the receiver operating characteristic (ROC) curve, since FPR is the complement of the sensitivity metric. While FNR decreases with the decision threshold, FPR increases when the decision threshold decreases. A high performance model must minimize the area below this curve, since this area is the complement of the area under the receiver operating characteristic curve (ROC AUC). The choice of $FPR_{isolation}$ and $FNR_{release}$ directly define the isolation and release probability thresholds respectively. The three triage configurations determine the distribution of COVID-19-positive and COVID-19-negative triage users into the three release-test-isolate triage categories (Fig. 1). Panels A, B, C correspond to the three triage configurations described in Table 1 and reflect a stable incidence period, a surge of infection, and a period with a decreasing incidence respectively.

Epidemic impact of the machine learning model

We simulated the impact of the agile triage model used in the context of outbreak control on the effective reproduction number (R_e), estimated in Belgium over the pandemic period [37]. We simulated how the ensemble model could reduce R_e, based on the values configured for the isolation and release thresholds. The epidemic impact is influenced by the proportion of immediately isolated cases among COVID-19-positive cases (isolation

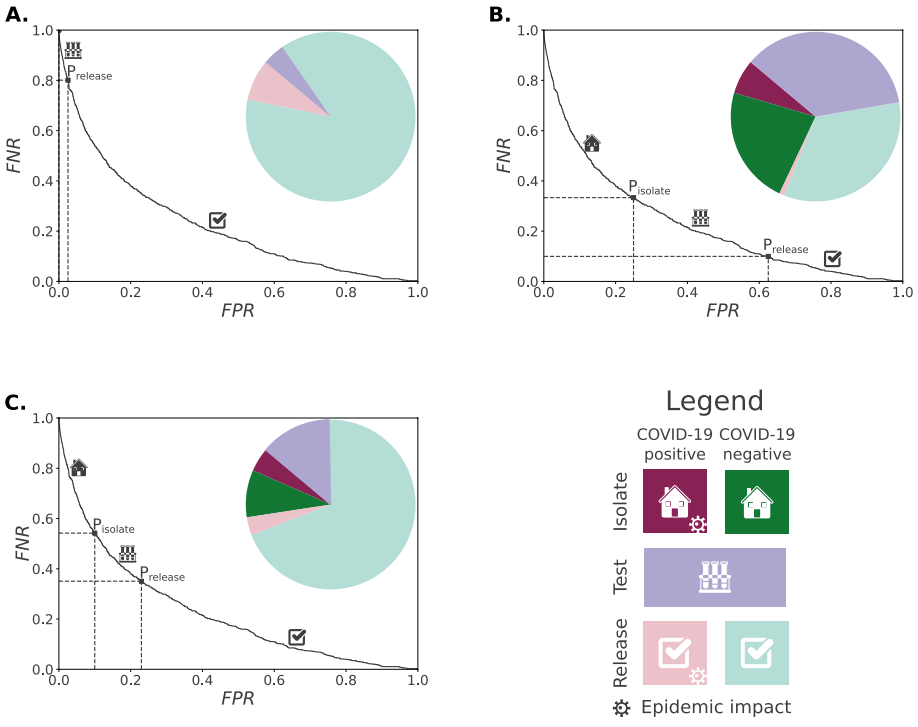

Fig. 1 Distribution of the population according to triage configurations. Each panel refers to one of the three triage configurations. Each panel shows the variation of one configuration metric (FNR) with the other (FPR), together with the triage probability thresholds $P_{release}$ and $P_{isolate}$. Each pie chart shows the distribution of COVID-19-positive and COVID-19-negative individuals within the release-test-isolate triage categories, determined by the triage configurations described in Table 1. In comparison to a traditional test-trace-isolate strategy which would test every individual requiring for a test, the ensemble-triage system has an epidemic impact which can be estimated from the proportion of the COVID-19-positive population who is isolated or released. (**A)** With a configuration of ($FPR_{isolation} = 0.00$, $FNR_{release} = 0.80$), no individual is isolated, and only few individuals at high risk on infections are tested. A considerable proportion of the population is released while being infected with COVID-19. (**B)** With a configuration of ($FPR_{isolation} = 0.25$, $FNR_{release} = 0.10$), 90% of COVID-19-infected cases are isolated or tested. 25% of the COVID-19-negative population is isolated. (**C)** with a configuration of ($FPR_{isolation} = 0.10$, $FNR_{release} = 0.35$), 35% of COVID-19-infected cases are isolated or tested. 10% of the COVID-19-negative population is isolated

sensitivity), and the proportion of released cases among COVID-19-positive cases ($FNR_{release}$). While the first group could reduce R_e by decreasing the delay before isolation, the second group contributes to propagating the virus and therefore increases R_e. We visualized how the sizes of those two groups impact R_e. This visualization is derived from the ROC curve (Supplementary Fig. B4).

We estimated the effect of the ensemble triage strategy on a given initial R_e with an existing test-trace-isolate (TTI) modeling framework. This compartmental model distributes the population into three different categories; infections detected through testing and subsequently isolated, quarantined contacts of COVID-19-positive cases and undetected infections within the community [3]. This model relies on different parameters, which are either disease-specific, or influenced by control measures in place (Supplementary Table C2). Among those, two parameters are influenced by the ensemble triage system:

- The average time delay from symptom onset to isolation in detected symptomatic cases. We assume that the triage model would reduce this delay by immediately isolating individuals within the population. Indeed, those individuals are not subject to the waiting delays between making an appointment for a PCR test and receiving the test result.
- The probability of detecting and isolating a case who perceived a risk of infection, which decreases when the triage system releases more individuals.

We estimated the effect of the ensemble triage system on R_e with a stochastic process and reported the interquartile range (IQR) of impacted values obtained over 1,000 simulations. We compared the impact of the ensemble triage strategy and the impact of the test-trace-isolate strategy that was implemented in Leuven on R_e, and on the number of tests performed. This latter strategy consisted in testing every individual who requested an appointment at the test center (all decisions to release or isolate individuals were made after testing, without any ensemble predictions). We simulated the implementation of ensemble-enhanced (with the three configurations) and ensemble-free strategies at the beginning of the Omicron BA.1 surge of infections. The ensemble-enhanced strategy was simulated by training the ensemble model on the data collected between September 20, 2021 and December 14, 2021 and testing the ensemble model on the data collected between December 15, 2021 and February 7, 2022. The testing delays used to configure the TTI modeling framework were recorded during the testing period. We considered an initial R_e of 1.09, as estimated in Belgium at the beginning of the testing (i.e. simulated triage implementation) period.

Results

Interpreting the machine learning results

The best predictive model was trained with the XGBoost algorithm, as implemented in the *xgboost Python* package. From the nested cross validation results, we obtained a mean ROC AUC of 77.5% ($SD = 0.9\%$) and a mean average precision (AP) of 33.4% ($SD = 0.4\%$). The AP is considerably higher than its chance level, i.e. the overall positivity rate at the test center ($SD = 9.9\%$). Indeed, the average precision is sensitive to the proportion of positive response variables within the data set. The other validated ensemble models achieved similar performance (Supplementary Table D3). The ROC AUC of the four-week ensemble models varies over time and is higher during periods of higher test center attendance, i.e. when more data are available to train the model (Fig. 2). This corroborates the evolution of the AP over time (Supplementary Fig. D5). A training heuristic that prioritizes

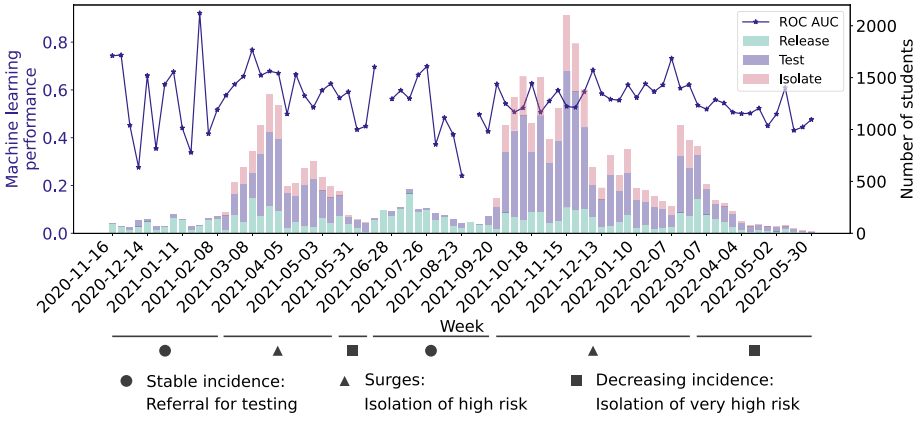

Fig. 2 Triage distribution of individuals with measures parametrized to control an outbreak (Table 1). The distribution of students in each triage category (release, test, isolate) varies with the configuration of the ensemble triage system. The weekly computed ROC AUC varies over time (left axis) and tends to increase when it is trained on more data, i.e. during the surges of infections during which testing demand is higher (March 2021 for instance). The model performance also influences the impact of the triage system on R_e (Supplementary Fig. I14)

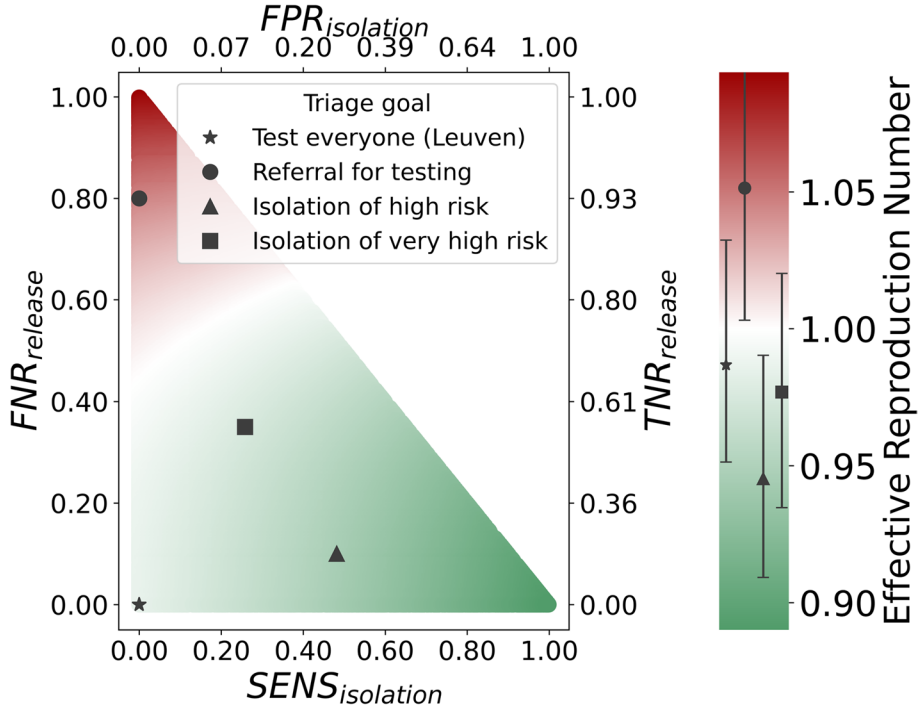

Fig. 3 Expected impact of triage for an initial $R_e = 1.09$ by isolation sensitivity and $FNR_{release}$. $SENS_{isolation}$ varies with $FPR_{isolation}$ (top axis) according to the shape of the ROC curve. The expected reproduction number is lower if the number of individuals isolated is higher and the number of individuals released is lower. The error bars represent the mean and IQR values of R_e computed based on stochastic simulations for the different triage measure configurations (described in Table 1)

the most recent data to train the model does not seem to significantly improve the performance of the ensemble model (Supplementary Figs. E6, E7).

The most influential predictors vary over the period of interest. At the beginning of the period, the reason why the individuals registered at the test center, the onset of symptoms, and the number of reported contacts influenced most the prediction of the model. Namely, the individuals were more likely predicted as positive if they had symptoms, a high risk contact or, surprisingly, if they reported a few number of contacts, which could reflect closer social interactions or their assessment of possible sources of infection. During the second half of the period, the vaccination status of the individuals influenced the predictions. However, since the vaccination coverage is high within the student population in Leuven, this variable may reflect the epidemic phase, rather than the immunity within the population (Supplementary Figs. F8, F9). Bayesian networks corroborate this interpretation (Supplementary Figs. F10, F11).

Epidemic control analysis

We simulated the implementation of the ensemble triage tool in the student population of Leuven to control an epidemic. The distribution of students within the three triage groups varies over time according to the configured values for $FNR_{release}$ and $FPR_{isolation}$ (Fig. 2). This figure represents two epidemic cycles observed during the COVID-19 pandemic. Those cycles involve three phases; a phase with a stable number of cases during which we configured the triage system to only test individuals at high risk of infection; followed by a surge of infections during which we configured the triage system with strict isolation measures; and ending with a phase of decreasing incidence during which we configured the triage system to alleviate isolation measure (Fig. 3).

Overall, this configuration of ensemble triage could have decreased the number of tests required by 47% $(= 17{,}715/37{,}705)$ between November 16, 2020 and May 31, 2022. This proportion varies over the course of the epidemic with regards to the choice of triage parameters. During stable incidence phases, triage could have saved 83% $(= 3{,}370/4{,}054)$ of tests. During surges of infections, most individuals would have been tested or isolated by triage while individuals with lower risk of infection would have been immediately released. Triage could have saved 42% $(= 12{,}680/30{,}114)$ of tests. During phases with a decreasing incidence, we would have isolated a minority of cases at high risk of infection and would have released a higher proportion of individuals than during surges of infections. Triage could have saved 47% $(= 1{,}665/3{,}537)$ of tests. With this measure, we would have only performed the few amount of necessary tests to distinguish between COVID-19-positive and COVID-19-negative

individuals with a mitigated risk of infection. We also studied the variation of the proportion of the number of tests saved with the two triage metrics $FNR_{release}$ and $FPR_{isolation}$ (Supplementary Fig. G12), and exemplified the use of the ensemble triage system for genomic surveillance. Our simulation suggests that the ensemble triage tool could reduce the number of tests required for this purpose by 16% (Supplementary Fig. H13).

Over the pandemic period, R_e varied over time. The pandemic was characterized by alternating phases of increasing incidence ($R_e > 1.0$) and phases of decreasing or stable incidence ($R_e \leq 1.0$). During our 84-weeks period of interest, R_e was estimated on average above 1.0 during 45 weeks. We simulated the epidemic impact of a rapid implementation of our triage system at the beginning of the Omicron BA.1 surge and we compared the impact of different triage measures. R_e was estimated at 1.09 at the beginning of the simulation period. During this period, a total of 658 cases were recorded and included in the analysis. When only testing individuals at high risk of infection, 0 cases would be isolated, 132 would be tested, and 526 would be released. Under strict isolation measures, 317 cases would be isolated, 275 would be tested, and 66 would be released. Under alleviated isolation measures, 170 cases would be isolated, 258 would be tested, and 230 would be released. Compared to the Leuven strategy of testing everyone at risk, we expect the rapidly isolated cases to further decrease R_e and the released infected cases to increase R_e.

When only testing individuals at high risk of infection, we expect the ensemble triage to decrease R_e to 1.04 ($IQR = [1.00, 1.09]$). With strict isolation measures, we expect to decrease R_e to 0.95 ($IQR = [0.91, 0.99]$). With alleviated isolation measures, we expect the ensemble triage to decrease R_e to 0.98 ($IQR = [0.93, 1.02]$). In comparison, this effect is similar to the expected impact that a traditional test-trace-isolate strategy would have, by testing the 658 cases. Indeed, we would expect the mitigation strategy as implemented in Leuven to decrease R_e to 0.99 ($IQR = [0.95, 1.03]$).

A rapid implementation of our triage system could have reduced R_e, potentially bringing it below one at the onset of an infection surge. However, the expected epidemic and test impact of the triage tool would have varied across the different variant of concern surges (Supplementary Fig. I14, Supplementary Tables I4, I5, I6, I7). Moreover, a delayed intervention may have led to the incapacity of the triage system to decrease R_e below 1.0 (Supplementary Fig. I15, Supplementary Tables I8, I9, I10).

Discussion

Diverse machine learning models achieved promising performance in predicting the risk of COVID-19 infection and severe illness [22, 23]. Notably, machine learning models were embedded within triage tools to predict severe illness and to distribute individuals into different risk categories at hospital admission [24–26]. Also, coordinated rapid response and active population screening were key to stabilizing epidemic morbidity and mortality [38]. In this study we propose a gradient boosting-enabled pre-test triage. Unlike previous studies, our triage decision is informed by in silico estimations of its impact on the effective reproduction number and the number of tests saved. Also, this triage is solely based on self-reported data, before any medical intervention, i.e. triage is implemented at the community level rather than at the hospital level. To our knowledge, such triage systems have received limited attention in the literature. We simulated a real-time implementation of this triage system in our student population. Our results suggest that ensemble models, when trained to predict the risk of infection, could help optimize triage before testing. By defining two adaptable probability thresholds, our system assigns release-test-isolate measures, based on self-reported individual data. This agile system could be used to optimally allocate testing resources during the different phases of an outbreak.

However, it should first be noted that the performance of the model strongly depends on the availability of data, and notably from cases with a positive PCR test, i.e. it depends on the positivity rate at the test center, which varies over time. While a low positivity rate can reflect a time-frame without many infections within a population, a high positivity rate underlines a high rate of unidentified cases within the community. A low positivity rate leads to strong data imbalance, and induces a bias towards COVID-19-negative individuals within the data set used to train the model. During periods with less infections, we would therefore suggest to train the ensemble model on a longer period than three weeks. Second, if a triage model would have been implemented over time, we would have only gathered data from individuals advised for testing by the model. We therefore would not have gathered the same individual data as we gathered with the testing strategy implemented in Leuven. We therefore emphasize that our analysis is a simulation, which can not perfectly represent a real-life implementation of the system we present. Third, to simplify the simulations, we defined probability thresholds based on the model tested during the fourth week. In practice, we would need to define and approximate the thresholds in advance to reach the targeted $FPR_{isolation}$ and $FNR_{release}$ metrics. Fourth, the epidemic impact of the model also depends on the compliance of the population to take a test or to isolate [39]. Finally, this study was also limited by the test-trace-isolate compartmental model. Namely, the epidemic impact computed is an estimation, which is inherent to the stochastic behavior

of this model. The model is also agnostic of social contact data and the age structure of the population. Contact matrices with age stratification help studying the effect of social interventions on an epidemic situation [40].

We showed that our analyses, albeit only presenting simulations, reflect high potential to optimize triage before testing. First, our results suggest that our agile triage system may efficiently decrease the workload and optimize the allocation of resources at the test center, while adapting to the successive epidemic waves. Second, we emphasize the restriction to the only use of self-reported data by the individuals during this study. We indeed did not train the model based on any data collected by health professionals, reflecting the autonomy, the rapidity, and the ease of use of our triage system. Third, we propose a framework to inform public health policy makers about the choice of adjustable triage measures based on the simulated impact of the ensemble triage system on the epidemic. Those triage measures can be adjusted based on two parametrizable metrics; the proportion of COVID-19-positive individuals we allow the model to release; and the proportion of COVID-19-negative individuals we allow the model to isolate. A rapid implementation of such a triage system may improve the control of an outbreak. A one-week-delayed implementation of the triage system could make this intervention inefficient. This would therefore require to either let the pathogen circulate or implement stronger social measures, such as a lockdown for instance.

In this study, we simulated a real-time implementation of the triage strategy by training each week a model based on the data gathered during the past few weeks. Further work must focus on validating the implementation of this triage framework in the population during a future outbreak. The predictive triage tool is compatible with any predictive binary classifier. We therefore suggest training an ensemble model (e.g. XGBoost) based on custom variables which reflect the risk of infection in the context of this particular outbreak. Better predictive performance could be achieved over time by training neural network architectures and fine-tuning those with recent data. The SAINT architecture proposed by Somepalli and colleagues shows promising performance [41]. Such models can be initially trained on a large data set, and regularly adapted according to the most recently gathered data [42]. Further work could also evaluate the effect of the triage system with an individual-based model and compare its result with compartmental models, like the one used in this study [43]. Finally, Obeid and colleagues have also predicted the individual risk of COVID-19 infection based on textual re-transcriptions of an interview given by a medical professional [44]. Combining ensemble models trained on structured data with large language models may therefore enhance triage.

Conclusions

In conclusion, despite variable performance over time, predicting the individual risk of infection could help define an adaptable release-test-isolate triage strategy for efficient allocation of tests. Our simulations suggest the potential of our triage tool to decrease the effective reproduction number within a given population. Predictive triage could also decrease the testing requirements at the test center.

Abbreviations

R_e	Effective reproduction number
AP	Average precision
COVID-19	Coronavirus disease 2019
CT	Computed tomography
ED	Emergency departments
FNR	False negative rate
FPR	False positive rate
ICU	Intensive care units
IQR	Interquartile range
ML	Machine learning
PCR	Polymerase chain reaction
ROC	Receiver operating characteristic
ROC AUC	Area under the receiver operating characteristic curve
RSV	Respiratory syncytial virus
SD	Standard deviation
TTI	Test-trace-isolate

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

JT and CG directly accessed and verified the data reported in this article. All authors had full access to the study data, critically reviewed the manuscript, and approved the final version. They all accept responsibility for submitting for publication. JT contributed to the conceptualization of the study, the data curation, the analysis, the visualization, the programming, the methodology, and the writing of the original draft. CG, EH, PL, KVD contributed to the methodology. EA contributed to the conceptualization of the study, the methodology, and the supervision.

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Data availability

The analysis scripts and anonymized data are available at https://github.com/jothibaut/ensemble_triage.git.
The Belgian meteorological data included within the analysis are available at https://opendata.meteo.be/download.
The Belgian epidemiological COVID-19 data included within this analysis are available at https://epidata.sciensano.be/epistat/dashboard/#data.
Individual-level health and social data cannot be shared to protect participant privacy and confidentiality.

Declarations

Ethics approval and consent to participate

The Ethics Committee Research UZ/KU Leuven approved the CT study protocol (approval number S64919). Informed consent was waived, as data collection was limited to public health purposes.

Competing interests

The authors declare no competing interests.

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