INTRODUCTION

Interference from weeds is a major threat to maize yield. Without any form of weed control, weeds cause higher yield losses than animal pests, pathogens, and viruses combined (Oerke, 2006). Average potential maize yield loss due to weed interference in the United States is 50%, threatening a domestic farmgate value of $26.7 billion (Soltani et al., 2016). Moreover, yield losses due to weeds are influenced by weather. Under drought conditions, numerous weed species exhibit increased competitiveness with maize (Patterson, 1995; Steckel & Sprague, 2004).

Soil-active and foliar-applied herbicides are central to modern weed management systems in maize. In 2018, 97% of all US maize hectares received one or more herbicide applications (USDA-NASS, 2021). Between 2008 and 2012, global producers spent roughly $26 billion annually on herbicides (Atwood & Paisley-Jones, 2017). Herbicide efficacy, determined empirically using a “weed control” rating system during the growing season, ranging from 0% (no weed control) to 100% (complete weed control), varies by product, application rate and timing, weed species, and environmental conditions. For instance, weed control failure is high with inadequate precipitation shortly after application of soil-applied herbicides (Landau et al., 2021). High temperatures hasten the growth rate of important weed species and reduce the amount of time that foliar-applied herbicides provide control (Guo & Al-Khatib, 2003). Additionally, the rate of...
herbicide metabolism (i.e., the conversion of an active herbicide to a less phytotoxic compound) within numerous weed species is positively correlated with temperature (Johnson & Young, 2002).

Achieving acceptable levels of weed control to prevent yield loss is becoming more difficult due to widespread herbicide resistance in weed populations. Herbicide resistance is defined as the inherited ability of a plant to survive and reproduce following exposure to a dose of herbicide that normally is lethal. Globally, 64 weed species commonly found in maize have evolved resistance to herbicides from most herbicide site-of-action groups commercially available in US maize production (Heap, 2021). Moreover, at least 16 of these species have evolved multiple herbicide resistance (i.e., resistance to two or more herbicides across different sites of action within the same population). The general sentiment about deteriorating herbicide efficacy among farmers is that new herbicide discovery will solve weed problems (Schroeder et al., 2018); however, increased costs of bringing new herbicides to market (Mcdougall, 2016) and a consolidation of the agrochemical industry to a few companies (Copping, 2018) have severely crippled herbicide discovery. For instance, three decades have passed since a new herbicide site of action was commercialized (Duke et al., 2019). Short of an unprecedented breakthrough in weed management technology, and widespread adoption of such technology, weeds will continue to interfere with maize well into the future.

Future weather is expected to be more variable and will significantly impact global maize yields. Global yearly average air temperatures are expected to rise 2.0–5.0°C by the year 2100 (Hayhoe et al., 2018). Additionally, the frequency of daily high temperatures ≥35°C is expected to increase over this period (Seneviratne et al., 2012). Increased daily average air temperature up to a threshold of 29°C improves maize yield; however, every 1°C increase beyond that threshold results in 1%–2% yield loss (Urban et al., 2012). Higher temperatures expected by the end of the century are predicted to cause between 9% and 28% yield loss in maize (Zhao et al., 2017). Increased temperatures are especially damaging during maize silking as excessive heat reduces pollination and increases kernel abortion (Lizaso et al., 2018; Prasad et al., 2018). Yearly precipitation in the major maize-producing regions is predicted to increase and will come mostly in the form of higher frequency of extreme precipitation events; however, the temporal distribution of the precipitation may change and will vary by region (Hayhoe et al., 2018). Much of the United States, the world’s largest maize producer (FAOUN, 2021), is expected to have increased spring precipitation accompanied by reduced summer precipitation (Hayhoe et al., 2018; Romero-Lankao et al., 2014). Increased spring precipitation reduces the number of field working days and delays planting and crop emergence (Tomasek et al., 2017). Decreased summer precipitation interferes with flowering and pollination, reducing maize yields up to 40% (Çakir, 2004). Projections of climate change on maize have yet to account for weeds that escape control. Generally, model predictions of maize performance focus on how weather variables directly or indirectly affect crop growth, development, and yield (Ummenhofer et al., 2015; Urban et al., 2015). Adverse weather and weeds are major stressors of maize that often occur simultaneously; however, their net effect on maize remains an open empirical question.

An obstacle to investigating linkages between weed control and weather variability on maize yield has been the small number of environments (e.g., generally 2–6) from which to draw inferences. Here, we use machine learning techniques to query a data set of 205 multi-location herbicide efficacy trials conducted by the University of Illinois since 1992 that were combined with weather and crop management data associated with each trial. Illinois is the second largest maize-producing state in the United States and is situated in the heart of the Corn Belt, which supplies 35% of the global annual maize production (FAOUN, 2021). The objective of the study was to determine the most important relationships among weed control, weather variability, and crop management practices on maize yield loss due to weeds. We hypothesized that yield loss due to weeds is greatest when coupled with drought stress or excessive heat, particularly near maize silking.

### 2 | MATERIALS AND METHODS

#### 2.1 | Field trials

Since 1992, the Herbicide Evaluation Program (HEP) at the University of Illinois has conducted >3000 individual herbicide evaluation trials. Trials were conducted in numerous fields throughout Illinois, with most trials located at the University of Illinois’ primary field locations in DeKalb (41°55′46″N/88°45′1″W) and Urbana (40°4′31″N/88°14′31″W). The soil types in DeKalb were either a Flanagan silt loam (fine, smectitic, mesic Aquic Argiudolls), or a Drummer silty clay loam (fine-silty, mixed, mesic Typic Endoaquolls) averaging a pH of 6.1 and organic matter of 5.9%. The soils in Urbana were a Flanagan silt loam or a Drummer silty clay loam averaging a pH of 6.4 and an organic matter of 4.9%.

All trials were arranged as a randomized complete block design with three replications. Treatments varied between trials but often consisted of various herbicides (at different rates and combinations), spray adjuvants, and a nonchemical weedy check. Data collected in each trial included percent weed control (i.e., 0% is no weed control, 100% is complete weed control) for different species collected at multiple times in a growing season, percent crop injury (i.e., 0% is no injury, 100% is crop death), and for some trials, crop yield. In most cases, the naturally occurring weed populations were used for control ratings; however, in rare instances, weed seeds were sown in plots when there was spatial heterogeneity of a target species. Trials also contain information on the maize hybrid and crop seeding rate. FieldPro: Bio Data Management Software (Heartland Technologies Inc., 12491 E. 136th St., Fishers Indiana) was used to input and archive data from the individual trials into a single database (hereafter called the HEP database).

#### 2.2 | Database management

The HEP database was filtered to contain only trials conducted in Dekalb or Urbana that contained both weed control ratings and
maize yield. The number of weed control ratings recorded within a given treatment ranged from one individual time point to six time points throughout the growing season. To compare trials at similar time points in the growing season, one early-season (21–35 days after planting) and one late-season (63–77 days after planting) weed control rating were used for each treatment. In most cases, late-season weed control ratings were taken shortly after postemergence herbicide application. Season-long weed control was calculated as the average of the early- and late-season control ratings.

Competitive indices (CIs) for each weed species were obtained from WeedSOFT Decision Support System (University of Nebraska-Lincoln, PO Box 830915, Lincoln, NE). A CI describes the competitiveness of an individual weed species with maize. The CI values in WeedSOFT are calculated from locally conducted field research, regional field research, and/or expert opinion (Neeser et al., 2004). For each weed species, CI values are scaled relative to the most competitive weed with maize using the following equation (Coble & Mortensen, 1992):

$$CI_i = \frac{P(i)}{P(m)} \times 10$$  (1)

where $P(i)$ is the proportion of maize yield lost from a very low density of weed $i$ and $P(m)$ is the proportion of maize yield lost from a very low density of the most competitive weed species in maize. CIs range from 0 to 10 with 10 being the most competitive weed with maize. The CI does not account for weed population density; therefore, abundant density of a low CI weed (e.g., 2.0) can be damaging, too. Four of the seventeen weed species in this study did not have a reported CI in WeedSOFT; therefore, the CIs of these species were estimated from comparable species. Trials investigated many of the most problematic weeds of the US Corn Belt (Sarangi & Jhala, 2018; Van Wychen, 2020), including giant foxtail (Setaria faberi Herm.), giant ragweed (Ambrosia trifida L.), and waterhemp (Amaranthus tuberculatus (Moq.) J. D. Sauer) (Table 1). To reduce the dimensionality of the data set, species were grouped by CI based on each species’ competitive ability with maize. Weed control varied greatly throughout the 27 years of study. The CI group with the lowest mean season-long control was the CI-10 group (mean = 67% weed control), which included giant ragweed (Table S1). The CI group with the highest mean season-long control was the CI-0 group (mean = 93% weed control), which included henbit (Lamium amplexicaule L.) and common chickweed (Stelaria media (L.) Vill.). For all CI groups, the minimum and maximum recorded weed control was 0% and 99%, respectively.

Trial weed-free yield was added to each treatment within a trial and was calculated as the average yield for each treatment with ≥95% control for all evaluated weed species. Trials that did not contain any treatment with ≥95% were removed from the database. Following this removal process, the database contained 649 and 2891 individual observations from DeKalb and Urbana, respectively.

| CI group | Common name | Scientific name | CI | Number of observations |
|----------|-------------|-----------------|----|------------------------|
| CI-0     | *Henbit     | Lamium amplexicaule L. | 0.5 | 59                     |
| CI-0     | *Common chickweed | Stelaria media (L.) Vill. | 0.5 | 55                     |
| CI-1     | Common lambsquarters | Chenopodium album L. | 1.5 | 2964                   |
| CI-1     | Pennsylvania smartweed | Persicaria pensylvanicum (L.) M. Gomez | 1.5 | 1150                   |
| CI-1     | Dandelion   | Taraxacum officinale F. H. Wigg | 1.5 | 99                     |
| CI-2     | Horseweed   | Erigeron canadensis L. | 2.0 | 52                     |
| CI-2     | Common ragweed | Ambrosia artemisiafolia L. | 2.0 | 492                    |
| CI-2     | Giant foxtail | Setaria faberi Herm. | 2.0 | 3282                   |
| CI-2     | *Smooth pigweed | Amaranthus hybridus L. | 2.5 | 446                    |
| CI-2     | Redroot pigweed | Amaranthus retroflexus L. | 2.5 | 98                     |
| CI-2     | Waterhemp   | Amaranthus tuberculatus (Moq.) J. D. Sauer | 2.5 | 1353                   |
| CI-4     | Velvetleaf  | Abutilon theophrasti Medik. | 4.2 | 3036                   |
| CI-5     | *Jimsonweed | Datura stramonium L. | 5.5 | 180                    |
| CI-5     | Ivyleaf morningglory | Ipomoea hederacea Jacq. | 5.5 | 254                    |
| CI-5     | Tall morningglory | Ipomoea purpurea (L.) Roth | 5.5 | 1833                   |
| CI-5     | Common cocklebur | Xanthium strumarium L. | 5.5 | 1003                   |
| CI-10    | Giant ragweed | Ambrasia trifida L. | 10.0 | 325                    |

*Species were grouped by the range of competitive indices (CIs). For example, CI-0 contains the tested species with a CI in maize between 0.0 and 0.9.
Percent yield loss was calculated for each treatment within a trial using the following equation:

\[
\text{Percent yield loss} = \frac{\text{trial weedfree yield} - \text{individual treatment yield}}{\text{trial weedfree yield}} \times 100
\]  

(2)

An estimated silking date was calculated for every maize hybrid of each trial in the HEP database by using the U2U web-based growing degree day (GDD) calculator (MRCC, 2020) to estimate the GDD’s required to reach silking and comparing them with the GDD accumulated after planting. Six consecutive 21-day intervals were created for each trial, with the third interval (interval 3) centered at the estimated silking date. Other time points coincided with the following maize growth stages: tassel initiation (interval 1), exponential growth (interval 2), kernel development (interval 4), grain fill (interval 5), and end of grain fill to physiological maturity (interval 6). Average air temperature, total rainfall, potential evapotranspiration (PET), and relative humidity were added to each trial for each of the 21-day intervals (data provided by the Illinois State Climatologist’s Office, a part of the Illinois State Water Survey located in Champaign and Peoria, Illinois, and on the web at www.sws.uiuc.edu/atmos/stateclim.). Cumulative GDDs and water balance were calculated and added to the 21-day intervals. The average vapor pressure deficit (VPD) was calculated for each 21-day interval using the following equation (Monteith & Unsworth, 2008):

\[
\text{VPD}_{avg} = 0.611 \times \exp \left( \frac{17.3}{T_{avg} + 237.3} \right) \times \left( 1 - \frac{RH_{avg}}{100} \right)
\]  

(3)

where \( T_{avg} \) and \( RH_{avg} \) are the average temperature and relative humidity, respectively, over the 21-day interval.

Typical of the US Corn Belt, large interannual variation in weather was observed. Season-long precipitation ranged from a minimum of 367 mm in 2005 to a maximum of 994 mm in 1993 (Table S1). Season-long PET ranged from 477 mm in 2009 to 890 mm in 2007. Average VPD during the 21-day intervals ranged from 0.20 to 1.33 kPa.

The database also captured a wide range of crop management practices. Although hybrids varied by trial, 50 maize hybrids were planted throughout the 27 years of trials. These hybrids were planted at densities ranging from 66,700 plants ha\(^{-1}\) in 1992 to 84,000 plants ha\(^{-1}\) in 2018 (Table S1). The density range in this study is consistent with average planting densities in Illinois over the same period (USDA-NASS, 2021). Depending on the year and planting date, the crop accumulated between 2772 and 3815 GDD throughout the growing season. Hybrids were planted from April 14 to June 3.

2.3 Statistical analysis

Classification and regression tree (CART) analysis was used to identify and visually model relationships among important weather, weed control, and crop management variables on maize yield and yield loss due to weeds. The CART analysis was conducted using the \texttt{rpart} package in R (Therneau & Atkinson, 2019). The CART algorithm continuously separates a dependent variable into two distinct subgroups, referred to as nodes, using categorical and continuous independent variables as splitting criteria and displays the final model as a dichotomous tree (Breiman et al., 1984). Threshold values that best split the data were selected by the model for each independent variable based on the distribution of the data. Independent variables were retained in the model only if they minimize the heterogeneity of the dependent variable. Independent variables were then removed from the model following the “1-se” rule (Venables & Ripley, 2002), which selects the model within one standard error from the minimum model error to provide the most parsimonious final model. Additionally, the minimum number of observations required for a terminal node was set to 20. The final regression tree models predict maize yield and maize yield loss due to weeds from weather, weed control, and crop management variables.

We used random forest analysis to determine variable importance of the weather, weed control, and crop management variables as predictors of maize yield loss due to weeds and maize yield. The random forest algorithm creates numerous regression trees, which are aggregated into one final model. The random forest analysis was conducted using the \texttt{randomForest} package in R (Liaw & Wiener, 2002). The number of individual regression trees created by the random forest algorithm was set to 500. The regression trees were created similar to CART analysis; however, a random subset of observations and independent variables was selected to construct each tree. Each subset of data was then split at random, with two-thirds of the data being used as a training set from which the tree is created, and the remaining one-third of the data being used as a hold-out set of data used to test the tree. During the tree-building process, the prediction error, or mean-squared error (MSE), on the hold-out set of data, was calculated for each tree (Breiman, 2001). The MSE was again recorded after permuting each independent variable within the tree. The importance of each variable was calculated as the difference between the two MSEs averaged across all trees divided by the standard error. Independent variables with a larger difference in MSEs are more important in predicting the dependent variables, whereas independent variables with smaller and negative differences are less important.

Both CART and random forest are nonparametric machine learning techniques that provide several advantages over traditional statistical methods such as linear or logistic regression. Both models make no assumptions about the distribution of the data and as such, do not require any data transformations. Additionally, CART and random forest are capable of handling numerous quantitative and qualitative independent variables and selecting those most important for predicting a specified dependent variable. Lastly, CART and random forest are useful when the data are unbalanced, or
data are missing. The 69 potential independent variables used in the CART and random forest models are shown in Table 2.

3 | RESULTS

Late-season control of all weed species was identified using random forest analysis as the most important predictor of maize yield loss due to weeds (Figure 1). Additional important variables for predicting maize yield loss included: late-season control of the CI-2 and CI-5 weeds, average temperature and VPD during silking, total rainfall during exponential growth, and planting date. The final random forest model explained 71% of the variability in maize yield loss due to weeds.

The final CART model predicting maize yield loss due to weeds included nine nodes and seven of the 69 potential independent variables: late-season average control of all weed species, late-season control of CI-2 group weeds, total rainfall during the exponential growth stage, VPD during silking, average air temperature during both tassel initiation and during silking, and planting date (Figure 2). All variables selected by the CART model were included in the 10 most important variables in the random forest model. The final CART model explained 61% of the variability in maize yield loss due to weeds. The highest average yield loss (i.e., 75% yield loss) was observed in treatments in which late-season control of all weeds was <12%, VPD during silking was ≥0.93 kPa, and temperature during tassel initiation was <21°C. The lowest average yield loss (i.e., 3% yield loss) was seen in treatments with ≥94% average late-season control of all weed species.

The random forest model predicting maize yield identified many of the same variables selected by the model for maize yield loss due to weeds (Figure S1). The final random forest model explained 70% of the variability in maize yield. The maize yield CART model included seven nodes and seven of the 69 potential independent variables explained 63% of the variability in maize yield (Figure S2). All variables selected by the yield CART model were included in the 10 most important variables in the random forest model. The lowest yields (i.e., 6289 kg ha$^{-1}$) occurred when late-season control of CI-2 group weeds was <72% and VPD during silking was ≥0.92 kPa.

| TABLE 2 | List of variables used in machine learning techniques |
| Variable group | Variables |
|----------------|-----------------------------------------------|
| Early-season weed control | Control of each species (%) |
| | Average control of each CI group (CI-0 to CI-5) |
| Late-season weed control | Control of each species (%) |
| | Average control of each CI group |
| Season-long weed control | Control of each species (%) |
| | Average control of each CI group |
| Air temperature | Season-long, daily thermal time (GDD) |
| | Maximum temperature during tassel initiation, exponential growth, silking, kernel development, grain fill, and physiological maturity (°C) |
| | Average temperature during tassel initiation, exponential growth, silking, kernel development, grain fill, and physiological maturity (°C) |
| Water | Total precipitation during tassel initiation, exponential growth, silking, kernel development, grain fill, and physiological maturity (mm) |
| | Potential evapotranspiration during tassel initiation, exponential growth, silking, kernel development, grain fill, and physiological maturity (mm) |
| | Water balance at tassel initiation, exponential growth, silking, kernel development, grain fill, and physiological maturity (mm) |
| | Vapor pressure deficit during tassel initiation, exponential growth, silking, kernel development, grain fill, and physiological maturity (kPa) |
| Crop management | Cultivar |
| | Previous crop |
| | Planting density (plants ha$^{-1}$) |
| | Days to silking |
| | Days to physiological maturity |
| | Planting date |
| | Crop injury (%) |
| | Herbicide treatment timing (i.e., PRE, POST, PRE+POST) |

Abbreviations: POST, postemergence; PRE, preemergence.
FIGURE 1  Random forest variable importance for predicting maize yield loss due to weeds. A larger percent increase in mean-squared error indicates a larger contribution of that variable for accurately predicting maize yield loss due to weeds. Only the 10 most important variables from those analyzed (Table 2) are shown. Explanation of abbreviations: CI-2, the average percent control of all species with a competitive index between 2.0 and 2.9; VPD, vapor pressure deficit; CI-5, the average percent control of all species with a competitive index between 5.0 and 5.9.

FIGURE 2  Final classification and regression tree for maize yield loss due to weed interference. Mean yield loss and number of observations are reported under each node and each leaf. A total of 3540 observations obtained from trials conducted between 1992 to 2018 were used to create the final tree model. Explanation of abbreviations: % YL, percent yield loss due to weeds; CI-2, the average percent control of all species with a competitive index between 2.0 and 2.9; % WC, percent weed control; VPD, vapor pressure deficit.
highest yields (i.e., 12,462 kg ha$^{-1}$) occurred when CI-2 late-season control was ≥72%, planting was ≥70,400 plants ha$^{-1}$, and water balance during the exponential growth stage was ≥−2 mm.

4 | DISCUSSION

Of the 69 potential variables accounting for maize yield loss, late-season control of all weed species was identified as the most important predictor of maize yield loss by both the CART and random forest models. Treatments with poor late-season weed control (<12%) had on average 50% yield loss compared with those treatments with higher levels of control (Figure 2). These results are consistent with recent work reporting 50% and 51% yield loss potential due to uncontrolled weeds in the United States and Illinois, respectively (Soltani et al., 2016).

In addition to late-season control of all weeds, late-season control of the CI-2 weed groups was one of the most important factors for predicting maize yield loss. Average maize yield loss was 25% when control of CI-2 weeds was <54% (Figure 2). Similarly, control of the CI-2 weeds also was important for predicting maize yield, and maize yields were on average 6000 kg ha$^{-1}$ higher when their control was ≥72% (Figure S2). Although the CI-2 weeds individually are less competitive with maize than higher CI groups (e.g., CI-3 and up), dense infestations are destructive. Certain CI-2 weeds, namely giant foxtail and waterhemp, are listed in the top 25% when control of CI-2 weeds was

As hypothesized, yield loss due to weeds is greatest when coupled with drought stress or excessive heat. Moreover, the period before and during maize silking was most sensitive to the combination of poor weed control and drought or excessive heat. Under the poorest levels of late-season weed control, treatments with higher VPD (≥0.93 kPa) during silking had on average 61% yield loss compared with 41% yield loss when VPD was lower (Figure 2). Additionally, high VPD during silking led to, on average, 2000 kg ha$^{-1}$ lower yields when late-season control of CI-2 weeds was low (<72%) (Figure S2). Even when moderate levels of weed control (12%–83%) were achieved, high average temperatures (≥26°C) during silking caused 20% greater yield loss compared with more moderate temperatures (<26°C). Furthermore, low rainfall (<5 mm) during exponential growth resulted in an average 12% yield loss even when relatively high levels of late-season weed control (84%–93%) were achieved. Higher yield loss due to weeds when water is limiting is likely due to increased competitiveness of several weed species for water under drought conditions (Patterson, 1995; Steckel & Sprague, 2004). Furthermore, above-average temperatures during silking exacerbate yield loss under drought conditions (Hu & Buyanovsky, 2003).

Changes in precipitation patterns and warmer temperatures are expected for much of the US Corn Belt over the coming century. Most of the region will experience reduced summer rainfall and higher instances of drought accompanied by an increase in average air temperature up to 5°C (Hayhoe et al., 2018; Romero-Lankao et al., 2014). Both drought and excessive temperatures around silking reduce maize flowering and pollination (Cañir, 2004; Lizaso et al., 2018; Prasad et al., 2018). These weather changes also will exacerbate the deleterious effect of weed competition on maize. In the current study, higher yield losses due to weeds were observed under water-limiting conditions and is likely caused by increased competition for the already limited water supply. Furthermore, warmer air temperatures increase the growth rate and competitiveness of waterhemp (Guo & Al-Khatib, 2003), green foxtail (Setaria viridis L.) (Wall, 1993), and Palmer amaranth (Amaranthus palmeri S. Wats) (Wright et al., 1999). As summer droughts and warmer temperatures become more common, the likelihood of maize experiencing the combined detrimental effects of heat stress, drought stress, and weed competition at the same time will increase. To limit the effects of these uncontrollable predicted weather changes on maize production, improvements in late-season weed control are essential.

The use of CART and random forest models in this study facilitated the selection of the most important weather, weed control, and crop management variables for accurately predicting maize yield loss due to weeds and maize yield. Both CART and random forest were chosen for this study due to fact that they have no assumption of normality and can use numerous quantitative and qualitative variables. The final CART models also are more easily interpreted compared with logistic or multiple regression techniques (Breiman et al., 1984), while random forest is capable of determining the importance of each independent variable for predicting maize yield loss due to weeds and maize yield (Breiman, 2001).
Overall, our study provides the most thorough assessment to date on the net effect of weed control and weather variability on maize yield. By using machine learning techniques on a database of herbicide evaluation trials spanning >3500 observations from 205 weather environments, this research provides insight into the consequences of weed interference on future maize yield. In the US Corn Belt, late-season weed control is essential; however, as herbicide resistance spreads, weed control will decline further. Given the linkages between poor weed control and dry, hot conditions on maize yield loss, yield projections assuming complete weed control are overestimated in rainfed production systems where drier, warmer conditions are expected. As global population and food demand rise over the coming century (UN-DESA, 2019), improving the efficacy of weed management systems is essential and will require transformational change in how weeds are managed to limit the destructive effects of predicted future weather on maize production (Harker, 2013; Westwood et al., 2017; Young et al., 2017).

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section.