Plant Breeding

WILEY

Plant Breeding

ORIGINAL ARTICLE OPEN ACCESS

Assessing Single-Trait and Multitrait Genomic Prediction Model Abilities Including Significant GWAS Markers for Fusarium Head Blight Disease Resistance in Wheat (*Triticum aestivum*)

Vinay Kumar Reddy Nannuru[1] | Jon Arne Dieseth[2] | Curt A. McCartney[3] | Maria Antonia Henriquez[4] | Hermann Buerstmayr[5] | Sebastian Michel[5] | Laura Morales[5,6] | Theodorus H. E. Meuwissen[7] | Jose Crossa[8] | Morten Lillemo[1]

[1]Department of Plant Sciences, Norwegian University of Life Sciences, Ås, Norway | [2]Graminor AS, Ridabu, Norway | [3]Department of Plant Science, University of Manitoba, Winnipeg, Manitoba, Canada | [4]Morden Research and Development Centre, Agriculture and Agri-Food Canada, Morden, Manitoba, Canada | [5]Institute of Biotechnology in Plant Production, Department of Agrobiotechnology, University of Natural Resources and Life Sciences Vienna, Tulln an der Donau, Austria | [6]Department of Forest Genetics and Plant Physiology, Swedish University of Agricultural Sciences, Umeå, Sweden | [7]Department of Animal and Aquacultural Sciences, Norwegian University of Life Sciences, Ås, Norway | [8]International Maize and Wheat Improvement Center (CIMMYT), Mexico City, Mexico

Correspondence: Morten Lillemo (morten.lillemo@nmbu.no)

Received: 28 June 2024 | **Revised:** 27 September 2024 | **Accepted:** 2 November 2024

Funding: This work was conducted as part of the SusCrop—ERA—NET project WheatSustain with funding for this study from the Research Council of Norway (NFR grant 299615), 'Bundesministerium für Nachhaltigkeit und Tourismus Österreich' (Forschungsprojekt Nr. 101402), the Genome Canada project CTAG2 and the Canadian Agricultural Partnership administered by the Canadian Wheat Research Coalition. The ERA-NET Cofund SusCrop (H2020 grant number 771134) is part of the Joint Programming Initiative on Agriculture, Food Security and Climate Change (FACCE-JPI). Additional internal funds for the present study were received from Graminor and NMBU.

Keywords: Fusarium head blight | genomic prediction | GWAS SNP covariates | multitrait | single trait | wheat

ABSTRACT

Disease resistance traits are complex and quantitative in nature. Breeders regularly evaluate multiple important traits across diverse environments to employ them in genomics-assisted breeding. In this study, we evaluated the prospects of genomic prediction models by incorporating genome-wide association study (GWAS) results into single-trait and multitrait genomic prediction scenarios, using two distinct panels: the NMBU panel and the GRAMINOR panel. A standard genomic prediction model (*Base*) and the Base model with the addition of significant GWAS markers as fixed covariates (Base + GWAS) were tested on both panels. The predictive ability of models was measured in terms of prediction ability by using Pearson's correlation method. An improvement of 0.05% to as high as a two-fold improvement was observed in both the panels for single-trait and multitrait scenarios. In general, multitrait models outperformed single-trait models regardless of whether the GWAS markers were included. This study further concludes that multitrait-based genomic predictions are superior to single trait–based ones when the associated traits are used and are well correlated.

Abbreviations: AE, anther extrusion; CV, cross-validation; DH, days to heading; DON, deoxynivalenol; FHB, Fusarium head blight; GEBVs, genomic estimated breeding values; GWAS, genome-wide association study; GS, genomic selection; MT, multi trait; PA, prediction ability; PH, plant height; ST, single trait.

1 | Introduction

Common wheat (*Triticum aestivum* L.) is an important and widely grown crop in Norwegian agriculture and globally. It is the second largest grown crop and serves as a staple food source worldwide, providing 20% of the calories in the human diet. Savary et al. (2019) estimated that global wheat yield losses due to biotic and abiotic stress average 21.5% (ranging between 10.1% and 28.1%). Among these factors, diseases and pests are one of the major contributors to these losses globally. For example, Fusarium head blight (FHB), which leads to poor seed quality and contamination of grains with harmful mycotoxins, is one of the most serious diseases attacking the wheat crop and causing huge losses in the final yield, predominantly in Europe and North America. The most important FHB-causing pathogen worldwide is *Fusarium graminearum*, which produces the mycotoxin deoxynivalenol (DON) (McMullen et al. 2012). FHB resistance is quantitative, with a complex genetic architecture greatly influenced by genotype-environment interactions. Therefore, replicated field experiments with reliable phenotypic selection are necessary for developing new cultivars with FHB resistance.

Climate change is one of the principal causes of disease epidemics, and FHB has become a major problem in present-day wheat cultivation. Both climate change and increasing food demand present challenges in wheat breeding, requiring rapid development and deployment of improved cultivars to adapt to changing ecological and economic conditions. Annual wheat production currently grows at a rate of 0.9%. However, with the global population expected to rise to 9 billion by 2050, annual global wheat production must increase by 2.4% to avoid a food shortage of 38% below the increased demand (Ray et al. 2013). Conventional breeding processes are time- and resource-consuming, and it typically takes around 10–12 years to develop a new cultivar. To accelerate breeding and reduce costs, novel approaches must be implemented into breeding programs. For example, the availability of high-density, low-cost marker genotyping platforms makes genomic prediction and selection feasible. Consequently, genomic selection (GS) can be implemented to predict breeding values of progeny lines without costly phenotyping, saving time and money while increasing the intensity and accuracy of trait selection (Meuwissen, Hayes, and Goddard 2001). Genomic prediction aims to utilize genetic resources, such as SNP markers, to predict the breeding values of new lines *in silico*. Combined with advanced data analysis, including machine learning and multitrait (MT) prediction models, GS can be a powerful tool for breeding, reducing the need for costly manual evaluation.

GS technology has already revolutionized animal breeding, where simulations and implementations have shown that the genetic gains can be doubled or even tripled (García-Ruiz et al. 2016). However, this potential has yet to be seen in plant breeding, despite over a decade of research into developing GS methodology for barley, maize, rice, sorghum and wheat for different traits of interest (Bernardo and Yu 2007; Zhong et al. 2009; Heffner et al. 2010; Heffner, Jannink, and Sorrells 2011; Lorenz, Smith, and Jannink 2012; Riedelsheimer, Technow, and Melchinger 2012; Zhao et al. 2012; Poland et al. 2012; Lorenz 2013; Rutkoski et al. 2014; Fernandes et al. 2018; Hunt et al. 2018; Spindel and Iwata 2018). In wheat breeding, considerable research has been carried out on yield and disease-resistance traits (Heffner, Jannink, and Sorrells 2011; Poland et al. 2012; Rutkoski et al. 2014; Jarquín et al. 2017; Jiang et al. 2017; Liu et al. 2021). Prediction accuracies are currently very low for complex diseases using GS. Therefore, in the current study, FHB will be used as a case to improve the prediction accuracies of disease resistance by use of significant and consistent QTL captured from our previous GWAS study (Nannuru et al. 2022).

To practice GS in a breeding program, a training population must be created that has been phenotyped for the traits of interest and genotyped with genome-wide markers. This training population provides phenotypic and genotypic information used to model a prediction equation (GS model), which predicts the marker effects on the traits. The GS model is then used to predict genomic estimated breeding values (GEBVs) on the testing set, which has only been genotyped for genome-wide markers and not phenotyped, to assess the predictive ability of the GS model. These GEBVs are used to make selective decisions on best-preforming genotypes in the breeding programs. Various statistical GS models have been developed over the past 20 years, with machine learning methods, both parametric and nonparametric, gaining popularity. Parametric methods include RR-BLUP (Meuwissen, Hayes, and Goddard 2001) and genomic BLUP (assuming a normal distribution of SNP effects), BayesA and weighted Bayesian shrinkage regression wBSR (assuming a prior normal distribution of effects with a higher probability of moderate to large effects) and BayesB and BayesCπ (assuming that some SNP effects are 0). Nonparametric methods include random forest, reproducing kernel Hilbert space (RKHS) or neural network approaches, and these models were compared by Heslot et al. (2012).

GS models typically consider the genetic marker's information or pedigree relationships for predictions both in animal and plant breeding programs. Incorporating GWAS-identified significant QTL markers in the GS models has improved prediction accuracies, particularly for complex traits. A model called GS + de novo GWAS where GWAS results are incorporated in prediction models has shown a superior performance to all the other models tested for various traits in different environments in rice (Spindel et al. 2016). Veroneze et al. (2016) demonstrated that including GWAS information in multipopulational genomic predictions has shown an increase in prediction accuracies in pigs. However, the use of GWAS markers as fixed covariates showed mixed results of prediction accuracies when predicting agronomic traits controlled by small-effect genes in maize and sorghum (Rice and Lipka 2019). Inclusion of haplotype-based GWAS loci as fixed effects in the prediction models resulted in a 9%–10% increase in prediction accuracies (Sehgal et al. 2020). Recent studies have shown similar results of an increase in prediction accuracies when GWAS results are included in the GS prediction models (Bian and Holland 2017; Liu et al. 2021; Ma and Cao 2021; Hao et al. 2022; Shahinnia et al. 2022; Morales et al. 2023, 2024). Most studies included GWAS results as fixed covariates for univariate genomic predictions and have seen increases in prediction accuracies. Furthermore, the inclusion of GWAS results and/or FHB-correlated traits as covariates in GS models has been previously shown to improve prediction accuracy for

FHB resistance in wheat (Arruda et al. 2016; Moreno-Amores, Michel, Löschenberger, et al. 2020; Moreno-Amores, Michel, Miedaner, et al. 2020; Larkin et al. 2020; Zhang et al. 2021; Akohoue et al. 2022; Morales et al. 2024). Our current study also focuses on the effect of GWAS-based QTL markers on prediction accuracies of both single-trait (ST) and MT models.

The objective of this study was to train different models and predict the breeding values for ST and MT models by incorporating the GWAS-based significant SNP markers as a fixed effect component into the genomic prediction models.

2 | Material and Methods

2.1 | Plant Material, Experimental Design and Trials

We obtained data from field trials on two wheat panels: the NMBU spring wheat panel (hereafter referred to as the NMBU panel) and the GRAMINOR spring wheat panel (hereafter referred to as the GRAMINOR panel). The NMBU panel is a collection of 296 hexaploid spring wheat accessions including lines mainly from Norway, Europe, the United States, CIMMYT (Mexico), China and Australia. The GRAMINOR panel consists of 358 new breeding lines from the commercial spring wheat breeding program of Graminor. The NMBU panel was tested over 5 years in four different locations, whereas the GRAMINOR panel was tested over 2 years in three locations.

Data was obtained from field trials at two locations in Norway: The Vollebekk research station at the Norwegian University of Life Sciences, Ås (59°N, 90 m above sea level), and the Staur research farm close to Hamar (60°N, 153 m above sea level). The NMBU panel was planted in α-lattice designs with two replicates at the Vollebekk research farm in 2013, 2014 and 2019 and at the Staur research farm in 2015. The GRAMINOR panel was evaluated in two replicates at the Vollebekk research station in 2020 and 2021, following the same methodology as for the NMBU panel.

In Austria, both panels were tested at the experimental station in the Department of Agrobiotechnology, Tulln, in 2020 (9°N, 177 m above sea level). In 2020, a subset of 200 lines from the NMBU panel was tested, whereas in 2021, the GRAMINOR panel was evaluated. Both trials in Tulln were conducted using randomized complete block designs with two replicates.

Both panels were also evaluated in a location in Canada at Morden, Manitoba. The NMBU panel was planted in an α-lattice design with two replicates in 2020, and in 2021, the GRAMINOR panel was tested following the same experimental design and methodology.

In the above-mentioned field trials, the lines from both panels were evaluated for FHB disease resistance–related traits such as FHB disease severity in the percentage of diseased spikelets and DON content in parts per million (ppm). Apart from these traits, other secondary traits were also recorded, such as plant height (PH), days to heading (DH) and anther extrusion (AE) (Table 1). For a more detailed description of how the field trials were conducted, the traits and how they were evaluated, please refer to Nannuru et al. (2022). Not all the traits were scored in each field experiment (Table 1).

TABLE 1 | List of environments (Year × Location) and phenotypic traits used for genomic prediction analysis: (a) the NMBU panel and (b) the GRAMINOR panel.

(a)

	Environment					
Trait	1	2	3	4	5	6
Anther extrusion	X	X	X	X		
Heading date	X	X	X	X	X	X
Deoxynivalenol	X	X	X	X	X	
FHB disease severity	X	X	X	X	X	X
Plant height	X	X	X	X	X	X

Note: Environment—2013_Vollebekk [1], 2014_Vollebekk [2], 2015_Staur [3], 2019_Vollebekk [4], 2019_Morden [5] and 2020_Tulln [6].

(b)

	Environment				
Trait	1	2	3	4	5
Anther extrusion	X		X		
Heading date	X	X		X	X
Deoxynivalenol	X			X	X
FHB disease severity	X	X	X	X	X
Plant height		X		X	X

Note: Environment—2020_Tulln [1], 2020_Vollebekk [2], 2021_Tulln [3] and 2021_Vollebekk [4], 2021_Morden [5]).

2.2 | DNA Extraction and Genotyping

Seedlings of the NMBU panel and GRAMINOR panel were grown in the greenhouse and genomic DNA was extracted from fresh young leaves using the DNeasy plant DNA extraction kit (Qiagen). The lines were genotyped using Trait Genetics Illumina 25 K SNP Chip and, in addition, genotyped with some KASP and SSR markers for key agronomic and disease resistance traits (Rasheed et al. 2016). The SSR markers were converted to a biallelic state and were filtered based on 10% missing data and a minor allele frequency of $\geq 5\%$ in the lines. Heterozygous genotypes were regarded as missing data. Positional information was assigned according to the Trait Genetics Illumina 25 K SNP Chip. After filtering and removing redundant markers, 21,652 markers remained in the genotype dataset. Imputation of the markers was done using the software Beagle 5.4 per the guidelines provided in the user manual (Browning, Zhou, and Browning 2018). Following the imputation, both genotypic datasets were merged to obtain the common markers between the panels using Plink 2.0 (Purcell et al. 2007). After the merging, 15,987 markers were common between the panels and kept for further use in the genomic prediction models.

2.3 | Phenotypic Data Analysis

Least square means (LSmeans) were calculated using the '*lme4*' package (Bates et al. 2014) and '*lmerTEST*' (Kuznetsova, Brockhoff, and Christensen 2017) in *R* (R Core Team 2021) for all the recorded phenotypic traits in this study. Models used for the calculation were based on the *lmer* function in the package '*lme4*' of R using REML. For alpha lattice design, Models 1 and 2 were used to calculate the LSmeans of single environments for each trait. For randomized complete block design, Models 3 and 4 were used to calculate the LSmeans of single environments and across the environments for each trait.

$$P_{iknl} = \mu + g_i + R_n + R{:}B_{kn} + e_{iknl} \quad (1)$$

and

$$P_{ijknl} = \mu + g_i + E_j + g \times E_{ij} + R_n + R{:}B_{kn} + e_{iJknl}, \quad (2)$$

where P_{iknl} is the phenotype (trait value) of the ith variety in the nth replicate in the kth block, μ is the general mean, g_i is the fixed effect of the ith variety, R_n is the random effect of the nth replicate, $R{:}B_{kn}$ is the random effect of the kth block within the nth replicate and e_{iknl} is the error term. In Model 2, P_{ijknl} is the phenotype (trait value) of the ith variety in the nth replicate in the kth block in the jth environment. μ is the general mean, g_i is the fixed effect of the ith variety, E_j is the random effect of the jth environment, $g \times E_{ij}$ is the random effect of the ith variety grown under the jth environment (interaction), R_n is the random effect of the nth replicate, $R{:}B_{kn}$ is the random effect of the kth block within the nth replicate and e_{ijknl} is the error term.

$$P_{inl} = \mu + g_i + R_n + e_{inl} \quad (3)$$

and

$$P_{ijnl} = \mu + g_i + E_j + R_n + g \times E_{ij} + e_{iJnl}, \quad (4)$$

where P_{inl} is the phenotype (trait value) of the ith variety in the nth replicate, μ is the general mean, g_i is the fixed effect of the ith variety, R_n is the random effect of nth replicate and e_{inl} is the error term. In Model 4, P_{ijnl} is the phenotype (trait value) of the ith variety in the nth replicate in the jth environment, μ is the general mean, g_i is the fixed effect of the ith variety, E_j is the random effect of the jth environment, $g \times E_{ij}$ is the random effect of the ith variety grown under the jth environment (interaction), R_n is the random effect of the nth replicate and e_{ijnl} is the error term.

Pearson correlations between the traits were calculated (Benesty et al. 2009) in *R* for both the panels and principal component analysis (PCA) biplot analysis was performed for all the traits using across-environment means in the R-package 'Factoextra' (Kassambara and Mundt 2017).

2.4 | Genotypic Data Analysis

PCA was performed to interpret the calculated eigenvalues and principal components by integrating the genotypic data from both panels using TASSEL software (Glaubitz et al. 2014). Additionally, marker combination analysis was conducted by evaluating the top associated GWAS markers selected for this study. This evaluation was based on the variation inflation factor (VIF) and correlation metrics. Low VIF and correlations between the markers were preferred. Marker combinations that showed improvement in prediction ability (PA) were retained and used for the analysis.

Linkage disequilibrium (LD) decay analysis was performed using TASSEL for the NMBU panel, the European set of the NMBU panel and the GRAMINOR panel. Genome-wide half-decay r^2 was estimated from the generated output from the software (Glaubitz et al. 2014).

Allele frequencies of GWAS-associated markers used for the NMBU panel, the European set of the NMBU panel and the GRAMINOR panel were calculated from the available genotypic data of the respective panels.

2.5 | ST and MT Genomic Predictions

We used the Bayesian ridge regression method, which is generally used for univariate and multivariate predictions implemented in the 'BGLR' package in R (Pérez and de los Campos 2014) with 5000 burn-in and 15,000 iterations for each trait. We fit the standard base genomic prediction model for ST and MT genomic predictions as follows:

$$y = \mu + Zu + e, \quad (5)$$

where y is the vector of phenotype on n genotypes for a single trait $(n \times 1)$; μ is the overall mean; Z is a design matrix with values of p markers on n number of genotypes $(n \times p)$; and $u_{(n \times 1)}$ is a predictor vector with $u \sim N(0, K_{(n \times n)}\sigma_g^2)$, where σ_g^2 is the additive genetic variance and K is the realized additive relationship matrix. The residuals e is a vector of residual error with $u \sim N(0, R_{(n\ x\ n)}\sigma_e^2)$, where R is the residual matrix and σ_e^2 is error variance. The same Model 5 was extended to multiple traits, where y is the vector of n genotypes for t multiple traits $(n \times t)$, μ is the overall mean for multiple traits, Z is a design matrix with genotype values of p markers on '$n \times t$' number of genotypes $[(n \times t) \times p]$; u is a predictor $[(n \times t) \times 1]$ was assumed to follow a distribution $u \sim MVN(0, \Sigma$ Ä $G)$, where Σ is a variance–covariance matrix across the multiple traits $(t \times t)$. The residuals e is a vector of residual error with $e \sim MVN(0, R$ Ä $I)$, where R is $(t \times t)$ variance covariance matrix of residuals in all traits and I is the identity matrix.

We used significantly associated markers as fixed covariates in another model called Base + GWAS for ST and MT. For this, the criteria chosen were using top significant markers across the environments and across the traits from the GWAS study by Nannuru et al. (2022). The model we fit is as follows:

$$y = \mu + X\beta + Zu + e, \quad (6)$$

where y is the vector of phenotype on n genotypes for an ST $(n \times 1)$, μ is the overall mean, β is the vector of fixed effects (significant markers from GWAS), X and Z are design matrices, u was assumed to follow a distribution described earlier in Model 5, and the rest of the factors are same as in Model 6. This model was used as MTBase + GWAS, where y is the vector of n

genotypes for t multiple traits ($n \times t$), μ is the overall mean, β is the vector of fixed effects (significant markers from GWAS), X and Z are design matrices, and the rest are same as described for Model 5.

The removal of top significant markers, utilized as fixed effects, from the overall markers used for calculating the additive relationship matrix (K) in Models 5 and 6 was ensured to prevent overfitting bias in the prediction models, as detailed by Spindel et al. (2016). The models are summarized in Table 2, and the top significant markers used in this study are summarized in Table 3.

The above-described models were used to make single trait and MT predictions with and without GWAS-associated SNP markers on both panels (the NMBU panel and the GRAMINOR panel) for all the single environments and across the environments. These models used for ST are referred to as STBase and the base model for MT predictions as MTBase, whereas the base models with SNP markers as fixed covariates for ST and MT predictions are referred to as STBase + GWAS and MTBase + GWAS. The GWAS-associated SNP markers used for both panels are solely based on GWAS output from the NMBU panel for both panels. This testing of prediction models on an independent panel of lines (the GRAMINOR panel) served as validation in this study. The associated markers were combined based on their demonstrated significant impact and influence on disease resistance, as identified in our previous allele stacking analysis (Nannuru et al. 2022).

TABLE 2 | Summary of the prediction models used in the study.

Model	Fixed effects	Relationship matrix
ST	—	$G_{Markers}$
ST + GWAS	GWAS markers	$G_{Markers-GWAS}$
MT	—	$G_{Markers}$
MT + GWAS	GWAS markers	$G_{Markers-GWAS}$

Note: Relevant GWAS markers were systematically excluded from the overall marker set for all analyses.

The FHB disease–related traits FHB disease severity and DON content were mainly used to evaluate the potential of the aforementioned models both for ST and MT scenarios. In the MT prediction scenario, AE, PH and DH were used as correlated traits to predict both FHB disease severity and DON content. Both the ST and MT prediction scenarios were assessed using the cross-validation method.

2.6 | Cross-Validations for Assessment of PA and Genomic Heritability

We employed a five-fold cross-validation methodology, which included 10 replications for each model evaluated across diverse environmental conditions. Within each fold of the replication process, phenotypic values associated with a specific trait were intentionally masked. During the cross-validation procedure, the model was iteratively run for 10 replications, resulting in the derivation of genomic estimated breeding values (GEBVs) for each masked fold. It is important to note that for ST prediction models, all traits to be evaluated were done simultaneously, with phenotypic values masked accordingly based on the predefined folds. Conversely, in MT prediction models, each trait was evaluated individually, with the phenotypic values of the target trait masked while retaining the phenotypic information from all other traits.

The NMBU panel and the GRAMINOR panel were alternatively used as training and validation sets to further evaluate the potential of the models tested in this study. The NMBU panel is further divided into 'European' and 'Others' based on the population structure analysis conducted by Nannuru et al. (2022). Consequently, the data were categorized into three groups: NMBU, GRAMINOR and European (the NMBU panel excluding 'Others'), which were alternately used for testing and validation purposes. The evaluation focused exclusively on a single trait scenario, and the results were reported accordingly.

PA was calculated as the Pearson correlation coefficient between predicted GEBVs and observed phenotypic values across

TABLE 3 | Summary of the top significant and associated GWAS markers used in the study.

SNP marker	Chromosome	Position (Mbp)	Included in
AX-94844681	3A	718	NMBU and GRAMINOR panels
wgrb619	3B	5	NMBU panel
wsnp_BG604678A_Ta_1_2	4A	582	NMBU panel
RFL_Contig1490_386	6A	605	NMBU and GRAMINOR panels
wsnp_Ex_c45713_51429315	6B	712	NMBU and GRAMINOR panels
Kukri_c57593_79	7A	702	NMBU and GRAMINOR panels

Note: Marker wgrb619 at the *Fhb1* locus has two alternative alleles, 730 (resistant allele) and 1450 (susceptible allele), and was not part of the genotyping procedure in the GRAMINOR panel, and marker wsnp_BG604678A_Ta_1_2 was missing in the GRAMINOR panel. Mbp = megabase pairs.

all folds and replications. This comprehensive assessment allowed us to effectively evaluate the performance of the models across different traits and environmental conditions, providing valuable insights into their predictive capabilities.

3 | Results

3.1 | Trait Correlations and Distributions

Pearson correlations between across-environment means of FHB disease severity with DON content in both panels showed high significance in both panels with $r = 0.64$ ($p < 0.0001$) in the NMBU panel and $r = 0.41$ ($p < 0.0001$) in the GRAMINOR panel. In both panels, AE was negatively correlated with DON content ($r = -0.53$ and -0.53, $p < 0.0001$) and FHB disease severity ($r = -0.58$ and -0.45, $p < 0.0001$) with high statistical significance. Some of the other correlations between trait means were highly significant in the NMBU panel, such as PH was negatively correlated with DON content ($r = -0.34$, $p < 0.0001$), whereas DH was positive and highly correlated with DON content ($r = 0.38$, $p < 0.0001$). In the GRAMINOR panel, similar trends were observed: PH was negatively correlated to DON ($r = -0.28$, $p < 0.0001$), and DH positively correlated to DON content ($r = 0.07$, $p < 0.0001$). The correlations of PH and DH to FHB were negligible in the GRAMINOR panel, but in the NMBU panel, the correlation between PH and FHB disease severity was highly significant ($r = -0.44$, $p < 0.0001$). These correlations are illustrated in the form of a PCA biplot, which visualizes negative and positive correlations between the traits (Figure 1).

Single environment and across the environments LSmeans of FHB disease severity and DON content showed continuous variation that resembled normal distributions. Considerable variation was observed within the NMBU panel, the European set of the NMBU panel and the GRAMINOR panel for the FHB disease severity and DON content both within environments and across the environments (Figure S1).

3.2 | PCA and Linkage Disequilibrium

PCA of the combined genotypic data from both panels revealed that the NMBU panel could be further categorized into European and exotic lines (others) using two principal components PC1 and PC2 accounting for 19.99% of the genetic variation (see Figure 2a), whereas PC1 and PC3 explaining 17.23% of the total variance revealed that others are quite noticeable in being genetically different from the European and Graminor lines (see Figure 2b).

Estimated half-decay r^2 varied between the panels and values ranged ($r^2 = 0.18–0.210$), with r^2 for half-decay in the NMBU panel was 0.18. For the European set of the NMBU panel, r^2 for half-decay was 0.19, and it was 0.21 for the GRAMINOR panel (Figure S3).

In addition to this, the allele frequencies for the GWAS-associated markers used for genomic prediction in the GRAMINOR and NMBU panels are shown in Figure S2.

3.3 | ST and MT Predictions

In general, incorporating GWAS markers as covariates led to an increase in PA. The extent of this improvement varied depending on whether the analysis was conducted within a single environment or across multiple environments, and it differed between the two panels studied. Specifically, while some cases within the GRAMINOR and NMBU panels did not exhibit an increase in PA when GWAS markers were used as fixed covariates, other scenarios did show notable improvements. Moreover, this trend was more consistently observed in MT scenarios. In some instances, the inclusion of GWAS-associated markers did not enhance PA. Despite these exceptions, the overall trend indicated that using GWAS markers as covariates generally enhanced PA.

The increase in PA ranged from as low as 0.05% to as high as a two-fold improvement. Altogether, the results exemplify that although the addition of GWAS markers can substantially enhance PA, the degree of improvement is variably dependent on the specific environment and panel under consideration (Figures 3, 4, 5 and 6; Figures S4, S5, S6 and S7). The results are elaborated below in context to analyses conducted with and without GWAS markers across the environments, traits and panels.

When using the European subset of the NMBU panel as training data to predict the GRAMINOR panel, the prediction of DON content performed well, whereas FHB disease severity showed negative PAs. Incorporating GWAS-associated markers, both individually and in combination, led to an increase in PA for both traits in the GRAMINOR panel (Figures 5 and 6; Figures S8 and S9; Table S3).

Furthermore, when the GRAMINOR panel was used as training data to predict the European subset of the NMBU panel, both traits did not perform well with and without GWAS-associated markers. In general, there was no difference observed between using individual markers versus marker combinations as fixed covariates in this context. Very similar patterns were observed when NMBU and GRAMINOR panels were used alternatively as training and validation sets (Figures 5 and 6; Figures S8 and S9; Table S3).

3.4 | Conventional Base Model (Base)

Overall, the MTBase PAs were considerably higher than those of the STBase models in both the NMBU and GRAMINOR panels. However, there were exceptions observed, particularly for the trait FHB disease severity in specific single environments [2021 Vollebekk within the GRAMINOR panel (Figures 3 and 4; Tables S1 and S2)].

These exceptions observed above were not observed in the NMBU panel (Figures 3; Figure S6; Tables S1 and S2). In most of the cases, MTBase models performed well compared to the STBase models across different single environments and across the environments (Figures 3 and 4; Figures S6 and S7). This pattern indicates that the superiority of MTBase models over STBase models was common across the traits and environments.

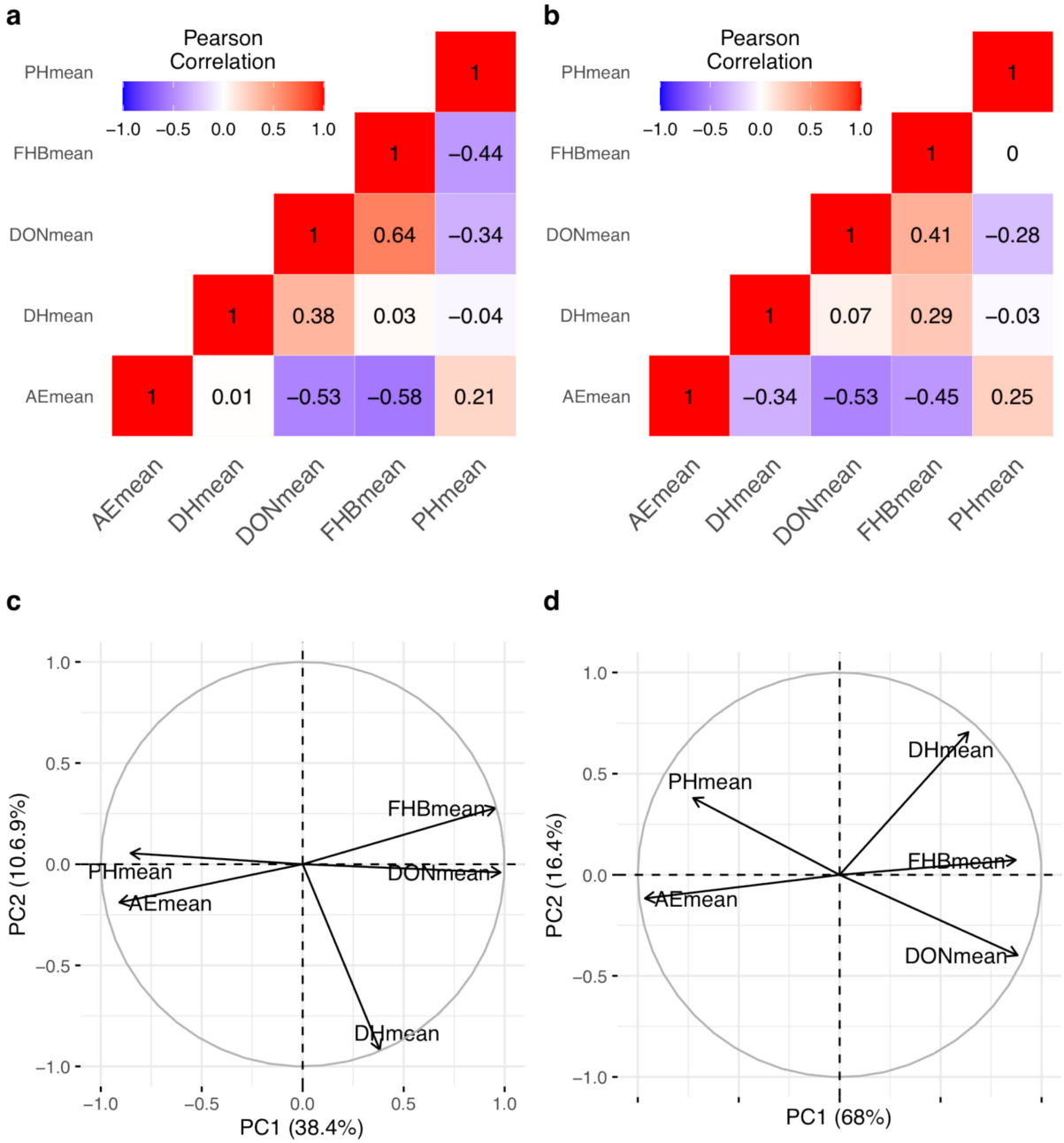

FIGURE 1 | Heatmap showing Pearson correlations between across-environment means of different traits for (a) the NMBU panel and (b) the Graminor panel. PCA—biplot explaining the correlation between the traits and genotypes for (c) the NMBU panel and (d) the Graminor panel. Abbreviation: PCA = principal component analysis. [Color figure can be viewed at wileyonlinelibrary.com]

3.5 | Base Model Plus GWAS Covariates (Base + GWAS)

In general, incorporating GWAS markers, whether individually or in combinations, led to an enhancement in PA both for STBase + GWAS and MTBase + GWAS models in both the NMBU and GRAMINOR panels (Figures 3 and 4; Figures S6 and S7; Tables S1 and S2). In general, more consistent effects of including GWAS markers were shown for MTBase + GWAS. The increases in PA were more prominent when individual markers were used compared to marker combinations in both the cases regarding traits as well as the environments for both panels (Figures 3 and 4). However, there were instances where combinations of GWAS-associated markers provided a more consistent improvement in PA. Notable examples include the marker combination 4A6B for both STBase + GWAS and MTBase + GWAS prediction models in the NMBU panel, and the marker combination 6A7A in the GRAMINOR panel (Figures S6 and S7; Tables S1 and S2).

Overall, MTBase + GWAS models demonstrated a more consistent increase in PA compared to STBase + GWAS models, both within single environments and across multiple environments, and for all the traits analysed in this study (Figures 3 and 4; Figures S6 and S7; Tables S1 and S2).

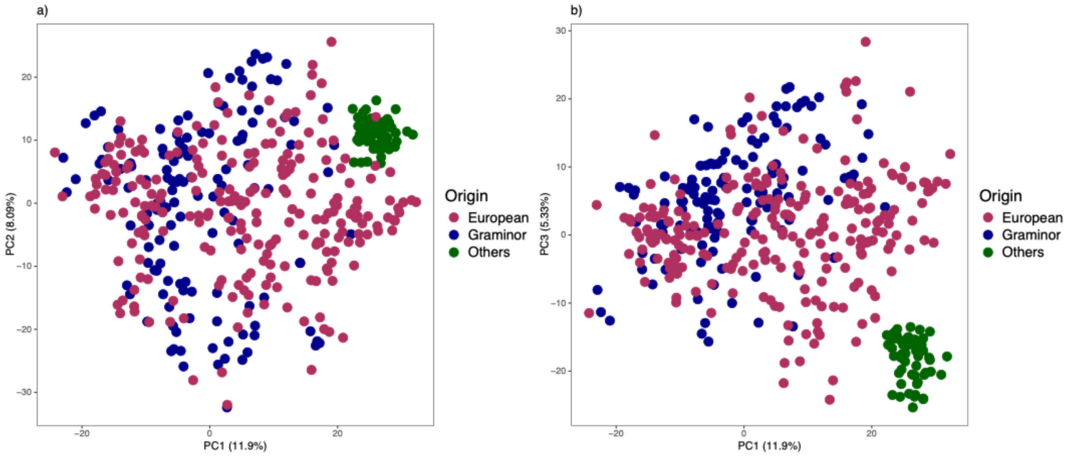

FIGURE 2 | Principal component analysis based on the 25 K data showing the population structure of the NMBU panel, which is divided mainly into two groups—European and others (lines from outside Europe such as from CIMMYT, China and the United States) and the GRAMINOR panel; (a) PC1 and PC2 and (b) PC1 and PC3. [Color figure can be viewed at wileyonlinelibrary.com]

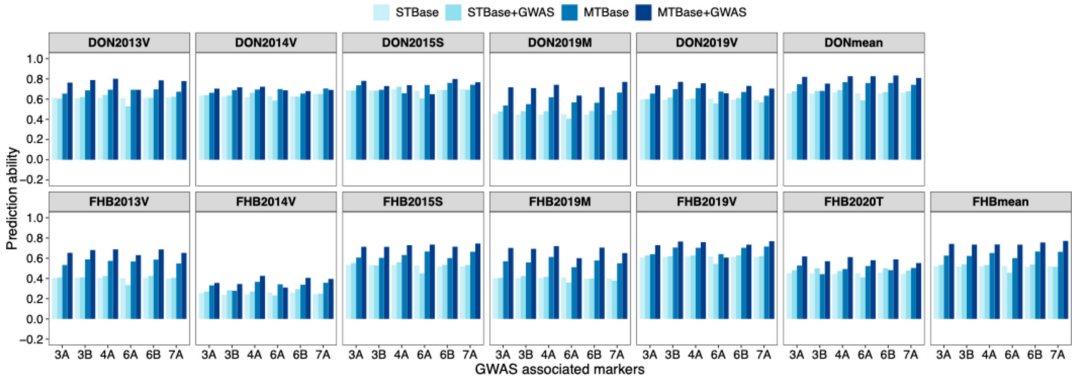

FIGURE 3 | Bar graphs showing the prediction abilities in single environments (Year × Location) and across-environment means of FHB disease severity and DON content using single-trait and multitrait prediction models in the NMBU panel. The *X*-axis labels indicate the chromosome from which significant GWAS-associated markers were used, and the *Y*-axis indicates the prediction ability of different genomic selection (GS) models tested. Abbreviations: FHB = Fusarium head blight, DON = deoxynivalenol; locations: M = Morden, S = Staur, T = Tulln and V = Vollebekk; mean = across-environment means; models: STBase = single-trait standard conventional GS model; STBase + GWAS = STBase + GWAS-associated markers as fixed covariates; MTBase = multitrait standard conventional GS model; MTBase + GWAS = MTBase + GWAS-associated markers as fixed covariates. [Color figure can be viewed at wileyonlinelibrary.com]

4 | Discussion

The main goal of implementing GS in plant breeding programs is to increase the PA of complex traits, making use of advances in the research area of genomics-assisted breeding. Breeders evaluate a wide variety of traits such as agronomic traits, grain yield, disease resistance and quality, among others; and these traits may be correlated. The number of traits evaluated together, as well as MT predictions, achieve better genetic gains. In this study, we evaluated correlated traits important for FHB disease resistance. Single trait and MT models were used to test genomic prediction models with and without GWAS covariates that were five-fold cross-validated with 10 replications. Our study's main aim was to evaluate the impact of PA in STBase + GWAS and MTBase + GWAS. We observed that there is a potential to increase the PA by the inclusion of GWAS markers. There was a considerable increase in PA in both the single trait model and MT models. However, the MT model PAs were higher than the single trait model's with and without the GWAS covariate in the prediction model. The reason for the good PAs in the MT model is due to the correlations between the traits and the established knowledge of the genetic architecture of FHB disease resistance. We also used the GRAMINOR panel as an independent material to test the models previously described. PAs were moderate to high, and there was an increase in PA when the GWAS-associated SNP markers were used with small exceptions. On the other hand, we also further tested the potential of the above-mentioned models using the NMBU panel as a whole, the 'European' subset of the NMBU panel and the GRAMINOR panel alternatively as training and validation sets in a more practical breeding context. More detailed aspects of the results will be discussed in the following.

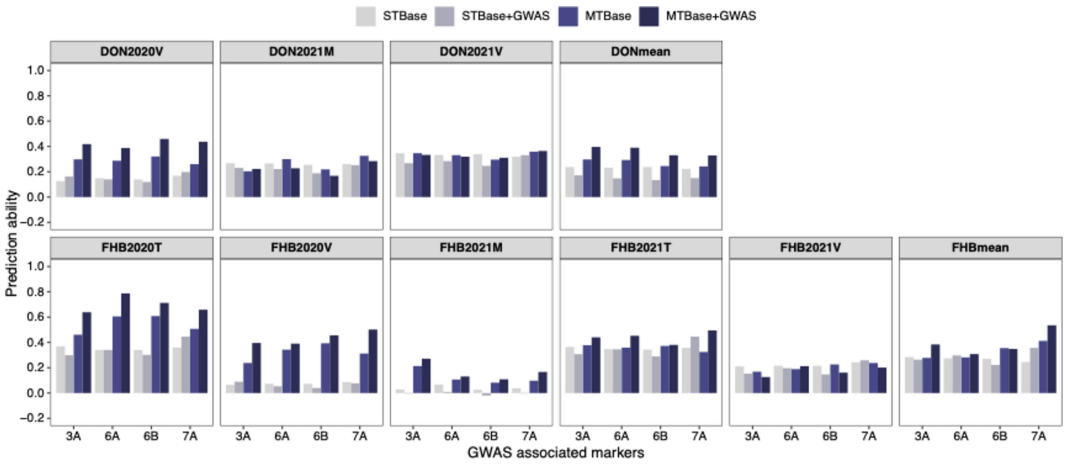

FIGURE 4 | Bar graphs showing the prediction abilities in single environments (Year × Location) and across-environment means of FHB disease severity and DON content using single-trait and multitrait prediction models in the GRAMINOR panel. The *X*-axis labels indicate the chromosome from which significant GWAS-associated markers were used, and the *Y*-axis indicates the prediction ability of different genomic selection (GS) models tested. Abbreviations: FHB = Fusarium head blight, DON = deoxynivalenol; locations: M = Morden, S = Staur, T = Tulln and V = Vollebekk; mean = across-environment means; models: STBase = single-trait standard conventional GS model, STBase + GWAS = STBase + GWAS-associated markers as fixed covariates; MTBase = multitrait standard conventional GS model; MTBase + GWAS = MTBase + GWAS-associated markers as fixed covariates. [Color figure can be viewed at wileyonlinelibrary.com]

4.1 | Trait Correlations and Genetic Diversity

Correlations between traits are very important, and they play a vital role in the MT model, as was also observed in our study. Traits associated with FHB disease resistance are well characterized, and the correlations from this study are in line with previous genetic studies. As we also observed, DH can be either negatively or positively correlated with FHB disease severity due to phenological differences in the germplasm and changing weather conditions during anthesis, which is the most susceptible stage for FHB infections (Andersen 1948; Sutton 1982; Kriss, Paul, and Madden 2010). A general negative correlation of FHB disease severity with PH is well established (Mao et al. 2010; Lu et al. 2013; Kubo et al. 2013), as also confirmed by our study. AE is an important trait evaluated for FHB disease resistance—the lower the value of AE, the higher the disease severity. Many studies (Skinnes et al. 2010; Lu et al. 2013; Kubo et al. 2013; Buerstmayr and Buerstmayr 2015; He, Lillemo, et al. 2016; He, Singh, et al. 2016) have reported a negative correlation between FHB disease and DON content with AE. The lines with high AE had lower infection rates, lower FHB disease severity and lower DON content. So, searching and selecting the genotypes with higher AE helps the breeding gains. AE, PH and DH are traits that have a direct influence on FHB disease and DON content since they affect the plant's susceptibility to the disease and these traits exhibit high heritabilities and are easy and cheap to score. For this reason, we used traits such as AE, DH and PH as correlated traits in MT prediction models in our study. The information from the correlated traits in the MT model was valuable and the PAs using this in the MT model were considerably higher. This was evident from our results in this study. Considering these trait correlations in the MT models and selecting the best genotypes will help achieve faster gains in a shorter time.

PCA of the NMBU panel and the GRAMINOR panel together explained a total variation of 19.99% from using the first two principal components; however, there was no remarkable difference seen among the three groups (European lines, Graminor lines and others; 'exotic lines'). But when PC3 was used instead of PC2, although the total variation decreased, a clear separation of exotic lines from the adapted European lines in the NMBU panel was apparent. Similarly, GRAMINOR lines displayed a bit more distinct grouping from the rest (Figure 2). This highlights the diversity present in the NMBU panel compared to adapted European lines from the NMBU panel and its distinction from the GRAMINOR panel. Furthermore, estimates of genetic diversity based on r^2 half-decay indicate that the NMBU panel exhibits a higher diversity compared to both the European set of the NMBU panel and the GRAMINOR panel. However, this difference is not considerably large, but it suggests that measurable levels of genetic diversity exist between the two panels.

4.2 | Impact of Adding GWAS Information to GS Model

Multiple studies in plant and animal breeding have incorporated GWAS results into the prediction models and reported increases in the PA. Sehgal et al. (2020) reported up to 9%–10% increase in PA by using the most consistent and robust associations from the GWAS conducted on genetic characterization of yield, and it was one of the first reports of integrating the trait genetic architecture in genomic prediction models for grain yield. They approached using GWAS-associated markers and haplotypes as fixed covariates in the prediction model for different environments with inclusion of epistatic effects. A study conducted on Eucalyptus tree breeding concluded that adding the GWAS results into the GS method was very valuable, as it enhances the power to identify the interesting and hidden potential of genomic variation in forest tree breeding (Tan and Ingvarsson 2022). They concluded that this method of incorporating the GWAS results into genomic

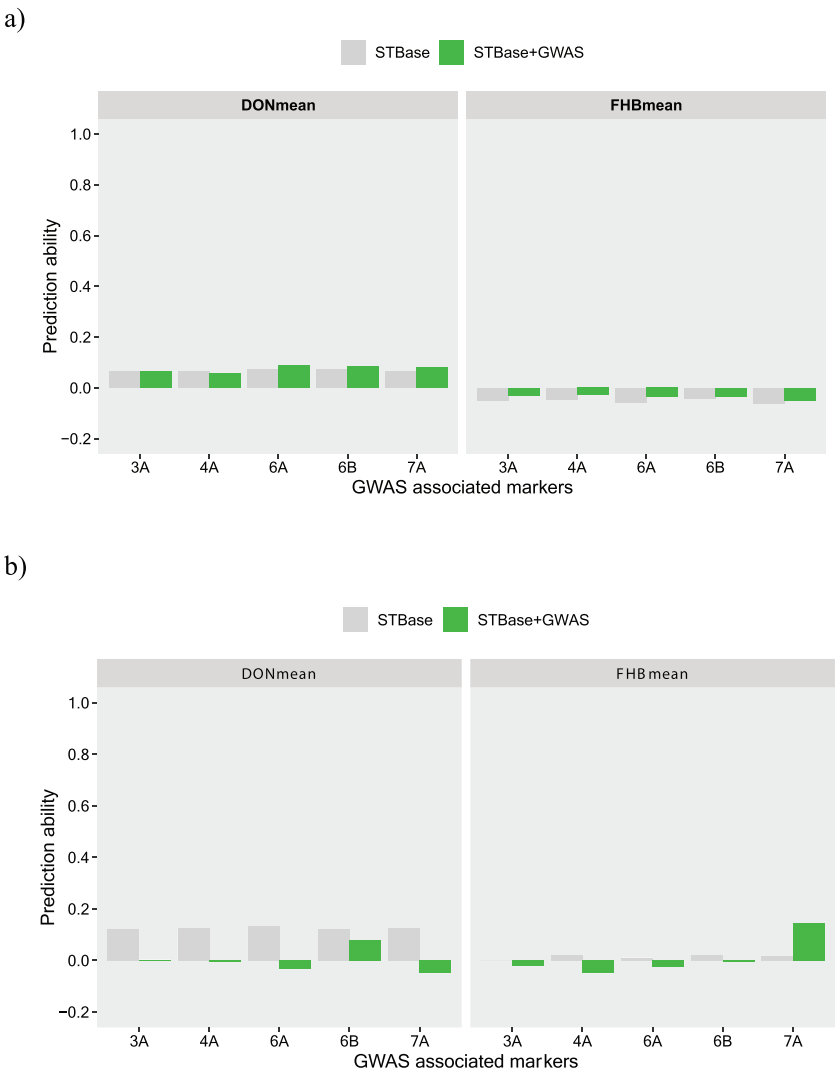

FIGURE 5 | Bar graphs showing the prediction abilities of across-environment means for FHB disease severity and DON content using single-trait GS prediction models, where NMBU and GRAMINOR panels were used alternately as training and validation sets: (a) 'NMBU' as a training set and 'GRAMINOR' as a validation set and (b) 'GRAMINOR' as a training set and 'NMBU' as a validation set. The *X*-axis labels indicate the chromosome from which significant markers were used, and the *Y*-axis indicates the prediction ability of different genomic selection (GS) models tested. Abbreviations: STBase = single-trait standard conventional GS model; STBase + GWAS = STBase + GWAS-associated markers as fixed covariates. [Color figure can be viewed at wileyonlinelibrary.com]

prediction improves the PA, which is a promising avenue to increase the efficiency of genomic predictions in forest tree breeding. Similar models were tested in a simulation study by Rice and Lipka (2019) in maize and sorghum. The idea was that GWAS peak significant markers could add and boost the PA in RR-BLUP models. They observed a reduction in PA and this reduction in PA was also seen in our study in some cases, whereas in most cases, there was an improvement. Similarly, including SNPs identified via GWAS as covariates in GBLUP models substantially improved PA for FHB resistance both within and across winter wheat breeding programs (Morales et al. 2024). In animal breeding, Veroneze et al. (2016) were one of the first ones to use computed weights from the GWAS results and apply these to multipopulational predictions. This showed an exceptional increase in the prediction accuracies; however, because this was performed in a single trait model, the results could potentially change under an MT model. They also mentioned that combining multiple traits would need new strategies to combine weights; otherwise, it is highly likely for a bias to occur in PA without these defined weights. Our study showed improved prediction performance with the use of MT models compared to ST models, and most cases with improved PA by the inclusion of GWAS markers were again MT models. We also assume that more training data and stronger correlations between traits will achieve a greater rise in PAs. The method of incorporating GWAS markers into GS was termed GS + de novo GWAS by Spindel et al. (2016). They performed this approach in rice breeding populations and reported that GS + de novo GWAS outperformed all the other models for several traits and in various environments. In addition to this, they proposed a two-part strategy breeding design which was used to bring new or novel genetic variation

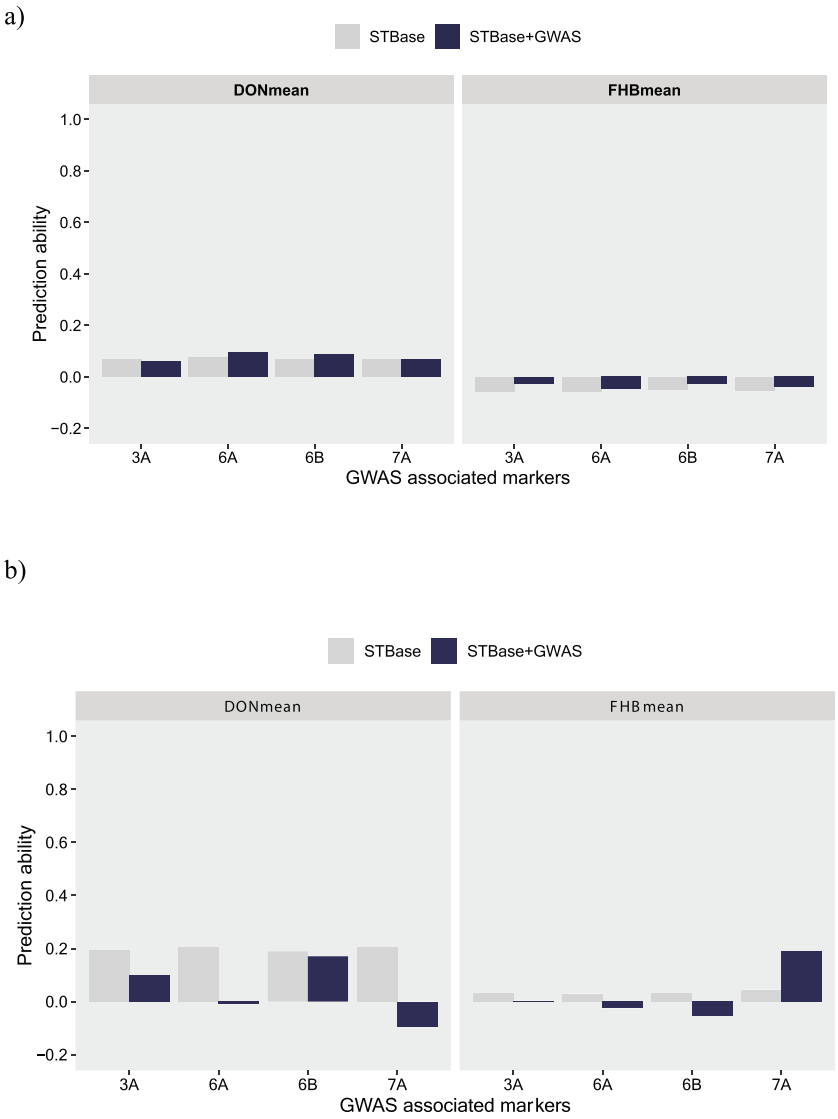

FIGURE 6 | Bar graphs showing the prediction abilities of across-environment means for FHB disease severity and DON content using single-trait GS prediction models, where European—(part of NMBU panel excluding 'Others') and GRAMINOR were used alternately as training and validation sets (NMBU panel was divided into 'European' and 'Others'): (a) 'European' as training set and 'GRAMINOR' as validation set and (b) 'GRAMINOR' as training set and 'European' as validation set. The *X*-axis labels indicate the chromosome from which significant markers were used, and the *Y*-axis indicates the prediction ability of different genomic selection (GS) models tested. Abbreviations: STBase = single-trait standard conventional GS model; STBase + GWAS = STBase + GWAS-associated markers as fixed covariates. [Color figure can be viewed at wileyonlinelibrary.com]

into elite breeding populations by adding more genetic diversity, thus increasing the potential chance of better genetic gains (Spindel et al. 2016). A simulation study has shown that having a major gene as a fixed effect in the prediction model was very beneficial, especially when the heritability and percentage of genetic variance explained by the gene is high. In contrast to this, when the major gene was used as a random effect and adding up a bulk of other markers, the PA decreased more quickly (Bernardo 2014). Some of these studies mentioned above served as an initial motivation to make use of GWAS associations in the genomic prediction models. Our results and observations are like those seen in previous studies. Furthermore, most of the cases showed a potential increase in genomic prediction abilities; however, this was not always the case for all traits and models tested in our study. We have observed a range of 0.05% to as high as a two-fold increase in the PAs. Elsewhere, it was mentioned that even a 1% increase in PAs achieved improved genetic gains (Bernardo 2014).

4.3 | MT Predictions Are Advantageous Over ST Predictions

The main aim of our study was to evaluate the potential of using the GWAS results in single trait and MT prediction models. MT models outperformed the ST models in PA when the Base model was used. This is because the association and correlations between different traits add up to the observed increase in the prediction accuracies. MT models were compared to ST models using different agronomic and malting

traits in barley (Bhatta et al. 2020). In the study, it was reported that MT predictions were always superior and outperformed the ST prediction model. CV1 and CV2 types were used for cross-validation purposes and MT-CV2 was better than the others (Bhatta et al. 2020). Nevertheless, we used five-fold cross-validation for assessing the PA and observed that the MT model is superior to the single trait model. There are only a limited number of studies conducted using multiple traits for predicting breeding values because of model complexity and the increased number of parameters involved. Most importantly accurate estimates of correlations between the MTs are needed for achieving better prediction abilities (Jia and Jannink 2012; Rutkoski et al. 2012; Montesinos-López et al. 2016; Lado et al. 2018). All the studies mentioned above reported advantages of MT prediction models, which use correlated MTs. Montesinos-López et al. (2016) reported that the MT model with correlated traits is better than uncorrelated traits. In our study, we evaluated the MT model using traits correlated with FHB disease resistance and observed an increase in PAs. Findings from our study emphasize that the variability in prediction accuracies varies between MT and ST base models across different traits and environments, highlighting the importance of considering trait-specific and environment-specific effects in genomic prediction studies. Alongside, it also highlights the complexity and variability inherent in genomic prediction and suggests that although MT models generally offer higher prediction accuracies, their performance can vary depending on the specific trait and environment. This shows the importance of considering both trait- and environment-specific effects in genomic prediction studies. Adopting a more nuanced approach that accounts for these factors can lead to more accurate and reliable genomic predictions, ultimately enhancing the application of GS in breeding programs. For example, considering genetic correlations between the traits, genetic architecture of the traits, environmental interactions, quality and quantity of data and most importantly model complexity and computational challenges are very important factors for consideration in general for GS prediction models (Meuwissen, Hayes, and Goddard 2001; Daetwyler, Villanueva, and Woolliams 2008; Heslot et al. 2012; Jia and Jannink 2012; Guo et al. 2014).

4.4 | Performance of Base and Base + GWAS Models on GRAMINOR Panel

Base + GWAS models in both ST and MT scenarios showed improvement in PAs for both the NMBU and GRAMINOR panels. But the idea of incorporating GWAS markers in the genomic prediction model for the GRAMINOR panel was considered a kind of validation, where no prior GWAS was conducted. We used the GWAS markers found significant in the NMBU panel and included those in the prediction models on the GRAMINOR panel. There was an increase in PA observed for STBase + GWAS and MTBase + GWAS, whereas there was a remarkable increase in the PAs in MTBase + GWAS compared to STBase + GWAS, which resembles the results observed from the NMBU panel. In our study, we have taken care of the overoptimization of GWAS markers and overfitting the GS models by systematically excluding the GWAS-associated markers from the overall genotypic marker set used to calculate the additive relationship matrix used, as followed and described in Spindel et al. (2016) and Li et al. (2019). However, on average, there was an increase in the PAs in STBase + GWAS and MTBase + GWAS. These results in the GRAMINOR panel suggest that GWAS-associated markers from the NMBU panel did contribute to the PA in GRAMINOR lines. This may be due to some associations of those GWAS markers used as fixed effects in this panel or some of the marker alleles that were fixed. We have used the robust and significant markers as detailed in Table 3. This approach to ensure that only robust QTLs that also segregate in the testing population are included as fixed effects could help to achieve higher PAs in most of the cases. Furthermore, there are other factors as mentioned in the previous section that contribute to the overall performance of the models. Additionally, we performed cross-population validation by using the NMBU panel as a training set and the GRAMINOR panel as a test set to evaluate the performance of Base and Base + GWAS models in the ST scenario. We observed a few cases of improved PAs for both FHB and DON content by the inclusion of GWAS markers. The usual scenario of improved PA was largely variable in cross-population validation of prediction models by inclusion of GWAS markers. Morales et al. (2024) recently reported that including GWAS SNPs and/or FHB-correlated traits in GBLUP models improved PA for FHB under both cross-validated and cross-population scenarios, further demonstrating that including GWAS markers identified in one population in GS modelling in another genetically related population can enhance PA. Our results indicate that the PA varies across different traits and panels when using GWAS markers, suggesting that the efficacy of genomic prediction models can depend on the specific genetic backgrounds and environmental conditions of the populations being studied.

5 | Conclusions and Outlook

We have evaluated the potential of incorporating GWAS-associated markers in genomic prediction models with the hypothesis of an increase in the PA based on promising results from previous studies. As hypothesized, inclusion of GWAS markers as fixed effects improved the PA, but this was dependent on which markers were used. Overall, the improvement was consistent in most cases for MT models. In general, MT models showed higher PAs and performed better than ST models. The increased predictive power of MT models likely comes from the use of genetic information from the correlated traits. When using GWAS markers from the NMBU panel in STBase + GWAS predictions on the GRAMINOR panel, improved PAs were seen in most cases. We conducted this study to explore the possibilities of improving the GS models by means of GWAS marker information. Most of the studies that used this approach were for ST models; we used this approach also in MT models with considerable success. However, in some cases, there was no success, which highlights the complexity of FHB disease resistance traits. Our study consequently concludes that MT models outperform ST models for predicting FHB disease resistance in wheat. Furthermore, it suggests the need for customized modelling strategies tailored to specific breeding objectives and environmental contexts to be used in predicting complex disease–related traits.

Author Contributions

Conceptualization: V.K.R.N. Data curation: V.K.N.R. Formal analysis: V.K.N.R. Funding acquisition: M.L. and J.A.D. Investigation: V.K.N.R., J.A.D., C.A.M., M.A.H., H.B., S.M., L.M., T.M. and M.L. Methodology: V.K.N.R., J.C., T.M. and M.L. Supervision: J.C., T.M. and M.L. Visualization: V.K.R.N. Writing – original draft: V.K.R.N. Writing – review and editing: V.K.R.N., J.A.D., C.A.M., M.A.H., H.B., S.M., L.M., J.C., T.M. and M.L.

Acknowledgements

This work was conducted as part of the SusCrop—ERA—NET project WheatSustain with funding for this study from the Research Council of Norway (NFR grant 299615), 'Bundesministerium für Nachhaltigkeit und Tourismus Österreich' (Forschungsprojekt Nr. 101402), the Genome Canada project CTAG2 and the Canadian Agricultural Partnership administered by the Canadian Wheat Research Coalition. The ERA-NET Cofund SusCrop (H2020 grant number 771134) is part of the Joint Programming Initiative on Agriculture, Food Security and Climate Change (FACCE-JPI). Additional internal funds for the present study were received from Graminor and NMBU.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The phenotypic and genotypic data are provided as supplementary material. Scripts and software used for data analyses in this study are available upon request. Other relevant information and supplementary material are attached to the manuscript submission.

References

Akohoue, F., S. Koch, J. Plieske, and T. Miedaner. 2022. "Separation of the Effects of Two Reduced Height (Rht) Genes and Genomic Background to Select for Less Fusarium Head Blight of Short-Strawed Winter Wheat (*Triticum aestivum* L.) Varieties." *Theoretical and Applied Genetics* 135: 4303–4326. https://doi.org/10.1007/s00122-022-04219-4.

Andersen, A. L. 1948. "The Development of *Gibberella zeae* Headblight of Wheat." *Phytopathology* 38: 595–611.

Arruda, M. P., A. E. Lipka, P. J. Brown, et al. 2016. "Comparing Genomic Selection and Marker-Assisted Selection for Fusarium Head Blight Resistance in Wheat (*Triticum aestivum* L.)." *Molecular Breeding* 36: 84. https://doi.org/10.1007/s11032-016-0508-5.

Bates, D., M. Mächler, B. Bolker, and S. Walker. 2014. "Fitting Linear Mixed-Effects Models Using lme4." ArXiv14065823 Stat

Benesty, J., J. Chen, Y. Huang, and I. Cohen. 2009. "Pearson Correlation Coefficient." In *Noise Reduction in Speech Processing*, edited by I. Cohen, Y. Huang, J. Chen, and J. Benesty, 1–4. Berlin Heidelberg, Berlin, Heidelberg: Springer.

Bernardo, R. 2014. "Genomewide Selection When Major Genes Are Known." *Crop Science* 54: 68–75. https://doi.org/10.2135/cropsci2013.05.0315.

Bernardo, R., and J. Yu. 2007. "Prospects for Genomewide Selection for Quantitative Traits in Maize." *Crop Science* 47: 1082–1090. https://doi.org/10.2135/cropsci2006.11.0690.

Bhatta, M., L. Gutierrez, L. Cammarota, et al. 2020. "Multi-Trait Genomic Prediction Model Increased the Predictive Ability for Agronomic and Malting Quality Traits in Barley (*Hordeum vulgare* L.)." *G3: Genes, Genomes, Genetics* 10: 1113–1124. https://doi.org/10.1534/g3.119.400968.

Bian, Y., and J. B. Holland. 2017. "Enhancing Genomic Prediction With Genome-Wide Association Studies in Multiparental Maize Populations." *Heredity* 118: 585–593. https://doi.org/10.1038/hdy.2017.4.

Browning, B. L., Y. Zhou, and S. R. Browning. 2018. "A One-Penny Imputed Genome From Next-Generation Reference Panels." *American Journal of Human Genetics* 103: 338–348. https://doi.org/10.1016/j.ajhg.2018.07.015.

Buerstmayr, M., and H. Buerstmayr. 2015. "Comparative Mapping of Quantitative Trait Loci for Fusarium Head Blight Resistance and Anther Retention in the Winter Wheat Population Capo×Arina." *Theoretical and Applied Genetics* 128: 1519–1530. https://doi.org/10.1007/s00122-015-2527-8.

Daetwyler, H. D., B. Villanueva, and J. A. Woolliams. 2008. "Accuracy of Predicting the Genetic Risk of Disease Using a Genome-Wide Approach." *PLoS ONE* 3: e3395. https://doi.org/10.1371/journal.pone.0003395.

Fernandes, S. B., K. O. Dias, D. F. Ferreira, and P. J. Brown. 2018. "Efficiency of Multi-Trait, Indirect, and Trait-Assisted Genomic Selection for Improvement of Biomass Sorghum." *Theoretical and Applied Genetics* 131: 747–755. https://doi.org/10.1007/s00122-017-3033-y.

García-Ruiz, A., J. B. Cole, P. M. VanRaden, et al. 2016. "Changes in Genetic Selection Differentials and Generation Intervals in US Holstein Dairy Cattle as a Result of Genomic Selection." *Proceedings of the National Academy of Sciences* 113: E3995–E4004. https://doi.org/10.1073/pnas.1519061113.

Glaubitz, J. C., T. M. Casstevens, F. Lu, et al. 2014. "TASSEL-GBS: A High Capacity Genotyping by Sequencing Analysis Pipeline." *PLoS ONE* 9: e90346. https://doi.org/10.1371/journal.pone.0090346.

Guo, G., F. Zhao, Y. Wang, Y. Zhang, L. du, and G. Su. 2014. "Comparison of Single-Trait and Multiple-Trait Genomic Prediction Models." *BMC Genetics* 15: 1–7. https://doi.org/10.1186/1471-2156-15-30.

Hao, X., A. Liang, G. Plastow, et al. 2022. "An Integrative Genomic Prediction Approach for Predicting Buffalo Milk Traits by Incorporating Related Cattle QTLs." *Genes* 13: 1430. https://doi.org/10.3390/genes13081430.

He, X., M. Lillemo, J. Shi, et al. 2016. "QTL Characterization of Fusarium Head Blight Resistance in CIMMYT Bread Wheat Line Soru# 1." *PLoS ONE* 11: e0158052. https://doi.org/10.1371/journal.pone.0158052.

He, X., P. K. Singh, S. Dreisigacker, S. Singh, M. Lillemo, and E. Duveiller. 2016. "Dwarfing Genes Rht-B1b and Rht-D1b Are Associated With Both Type I FHB Susceptibility and Low Anther Extrusion in Two Bread Wheat Populations." *PLoS ONE* 11: e0162499. https://doi.org/10.1371/journal.pone.0162499.

Heffner, E. L., J.-L. Jannink, and M. E. Sorrells. 2011. "Genomic Selection Accuracy Using Multifamily Prediction Models in a Wheat Breeding Program." *Plant Genome* 4: 65–75.

Heffner, E. L., A. J. Lorenz, J. Jannink, and M. E. Sorrells. 2010. "Plant Breeding With Genomic Selection: Gain per Unit Time and Cost." *Crop Science* 50: 1681–1690. https://doi.org/10.2135/cropsci2009.11.0662.

Heslot, N., H.-P. Yang, M. E. Sorrells, and J.-L. Jannink. 2012. "Genomic Selection in Plant Breeding: A Comparison of Models." *Crop Science* 52: 146–160. https://doi.org/10.3835/plantgenome2010.12.0029.

Hunt, C. H., F. A. van Eeuwijk, E. S. Mace, B. J. Hayes, and D. R. Jordan. 2018. "Development of Genomic Prediction in Sorghum." *Crop Science* 58: 690–700. https://doi.org/10.2135/cropsci2017.08.0469.

Jarquín, D., C. Lemes da Silva, R. C. Gaynor, et al. 2017. "Increasing Genomic-Enabled Prediction Accuracy by Modeling Genotype × Environment Interactions in Kansas Wheat." *Plant Genome* 10: plantgenome2016.12.0130. https://doi.org/10.3835/plantgenome2016.12.0130.

Jia, Y., and J.-L. Jannink. 2012. "Multiple-Trait Genomic Selection Methods Increase Genetic Value Prediction Accuracy." *Genetics* 192: 1513–1522. https://doi.org/10.1534/genetics.112.144246.

Jiang, Y., A. W. Schulthess, B. Rodemann, et al. 2017. "Validating the Prediction Accuracies of Marker-Assisted and Genomic Selection of Fusarium Head Blight Resistance in Wheat Using an Independent Sample." *Theoretical and Applied Genetics* 130: 471–482. https://doi.org/10.1007/s00122-016-2827-7.

Kassambara, A., and F. Mundt. 2017. "Package 'factoextra'." Extr Vis Results Multivar Data Anal 76.

Kriss, A. B., P. A. Paul, and L. V. Madden. 2010. "Relationship Between Yearly Fluctuations in Fusarium Head Blight Intensity and Environmental Variables: A Window-Pane Analysis." *Phytopathology* 100: 784–797. https://doi.org/10.1094/PHYTO-100-8-0784.

Kubo, K., M. Fujita, N. Kawada, et al. 2013. "Minor Differences in Anther Extrusion Affect Resistance to Fusarium Head Blight in Wheat." *Journal of Phytopathology* 161: 308–314. https://doi.org/10.1111/jph.12060.

Kuznetsova, A., P. B. Brockhoff, and R. H. Christensen. 2017. "lmerTest Package: Tests in Linear Mixed Effects Models." *Journal of Statistical Software* 82: 1–26. https://doi.org/10.18637/jss.v082.i13.

Lado, B., D. Vázquez, M. Quincke, P. Silva, I. Aguilar, and L. Gutiérrez. 2018. "Resource Allocation Optimization With Multi-Trait Genomic Prediction for Bread Wheat (*Triticum aestivum* L.) Baking Quality." *Theoretical and Applied Genetics* 131: 2719–2731. https://doi.org/10.1007/s00122-018-3186-3.

Larkin, D. L., A. L. Holder, R. E. Mason, et al. 2020. "Genome-Wide Analysis and Prediction of Fusarium Head Blight Resistance in Soft Red Winter Wheat." *Crop Science* 60: 2882–2900. https://doi.org/10.1002/csc2.20273.

Li, D., Z. Xu, R. Gu, et al. 2019. "Enhancing Genomic Selection by Fitting Large-Effect SNPs as Fixed Effects and a Genotype-by-Environment Effect Using a Maize BC1F3: 4 Population." *PLoS ONE* 14: e0223898. https://doi.org/10.1371/journal.pone.0223898.

Liu, Y., G. Hu, A. Zhang, et al. 2021. "Genome-Wide Association Study and Genomic Prediction of Fusarium Ear Rot Resistance in Tropical Maize Germplasm." *Crop Journal* 9: 325–341. https://doi.org/10.1016/j.cj.2020.08.008.

Lorenz, A. J. 2013. "Resource Allocation for Maximizing Prediction Accuracy and Genetic Gain of Genomic Selection in Plant Breeding: A Simulation Experiment." *G3 GenesGenomesGenetics* 3: 481–491. https://doi.org/10.1534/g3.112.004911.

Lorenz, A. J., K. P. Smith, and J.-L. Jannink. 2012. "Potential and Optimization of Genomic Selection for Fusarium Head Blight Resistance in Six-Row Barley." *Crop Science* 52: 1609–1621. https://doi.org/10.2135/cropsci2011.09.0503.

Lu, Q., M. Lillemo, H. Skinnes, et al. 2013. "Anther Extrusion and Plant Height Are Associated With Type I Resistance to Fusarium Head Blight in Bread Wheat Line 'Shanghai-3/Catbird'." *Theoretical and Applied Genetics* 126: 317–334. https://doi.org/10.1007/s00122-012-1981-9.

Ma, J., and Y. Cao. 2021. "Genetic Dissection of Grain Yield of Maize and Yield-Related Traits Through Association Mapping and Genomic Prediction." *Frontiers in Plant Science* 12: 690059. https://doi.org/10.3389/fpls.2021.690059.

Mao, S.-L., Y.-M. Wei, W. Cao, et al. 2010. "Confirmation of the Relationship Between Plant Height and Fusarium Head Blight Resistance in Wheat (*Triticum aestivum* L.) by QTL Meta-Analysis." *Euphytica* 174: 343–356. https://doi.org/10.1007/s10681-010-0128-9.

McMullen, M., G. Bergstrom, E. De Wolf, et al. 2012. "A Unified Effort to Fight an Enemy of Wheat and Barley: Fusarium Head Blight." *Plant Disease* 96: 1712–1728. https://doi.org/10.1094/PDIS-03-12-0291-FE.

Meuwissen, T. H. E., B. J. Hayes, and M. E. Goddard. 2001. "Prediction of Total Genetic Value Using Genome-Wide Dense Marker Maps." *Genetics* 157: 1819–1829. https://doi.org/10.1093/genetics/157.4.1819.

Montesinos-López, O. A., A. Montesinos-López, J. Crossa, et al. 2016. "A Genomic Bayesian Multi-Trait and Multi-Environment Model." *G3: Genes, Genomes, Genetics* 6: 2725–2744. https://doi.org/10.1534/g3.116.032359.

Morales, L., C. Ametz, H. G. Dallinger, et al. 2023. "Comparison of Linear and Semi-Parametric Models Incorporating Genomic, Pedigree, and Associated Loci Information for the Prediction of Resistance to Stripe Rust in an Austrian Winter Wheat Breeding Program." *Theoretical and Applied Genetics* 136: 23. https://doi.org/10.1007/s00122-023-04249-6.

Morales, L., A. Denis, G. Anne-laura, et al. 2024. "Leveraging Trait and QTL Covariates to Improve Genomic Prediction of Resistance to Fusarium Head Blight in Central European Winter Wheat." *Frontiers in Plant Science* 15: 1454473. https://doi.org/10.3389/fpls.2024.1454473.

Moreno-Amores, J., S. Michel, F. Löschenberger, and H. Buerstmayr. 2020. "Dissecting the Contribution of Environmental Influences, Plant Phenology, and Disease Resistance to Improving Genomic Predictions for Fusarium Head Blight Resistance in Wheat." *Agronomy* 10: 2008.

Moreno-Amores, J., S. Michel, T. Miedaner, C. F. H. Longin, and H. Buerstmayr. 2020. "Genomic Predictions for Fusarium Head Blight Resistance in a Diverse Durum Wheat Panel: An Effective Incorporation of Plant Height and Heading Date as Covariates." *Euphytica* 216: 1–19. https://doi.org/10.1007/s10681-019-2551-x.

Nannuru, V. K. R., S. S. Windju, T. Belova, et al. 2022. "Genetic Architecture of Fusarium Head Blight Disease Resistance and Associated Traits in Nordic Spring Wheat." *Theoretical and Applied Genetics* 135: 2247–2263. https://doi.org/10.1007/s00122-022-04109-9.

Pérez, P., and G. de los Campos. 2014. "BGLR: A Statistical Package for Whole Genome Regression and Prediction." *Genetics* 198: 483–495. https://doi.org/10.1534/genetics.114.164442.

Poland, J., J. Endelman, J. Dawson, et al. 2012. "Genomic Selection in Wheat Breeding Using Genotyping-by-Sequencing." *Plant Genome* 5: plantgenome2012.06.0006. https://doi.org/10.3835/plantgenome2012.06.0006.

Purcell, S., B. Neale, K. Todd-Brown, et al. 2007. "PLINK: A Tool Set for Whole-Genome Association and Population-Based Linkage Analyses." *American Journal of Human Genetics* 81: 559–575. https://doi.org/10.1086/519795.

R Core Team. 2021. "R: A Language and Environment for Statistical Computing."

Rasheed, A., W. Wen, F. Gao, et al. 2016. "Development and Validation of KASP Assays for Genes Underpinning Key Economic Traits in Bread Wheat." *Theoretical and Applied Genetics* 129: 1843–1860. https://doi.org/10.1007/s00122-016-2743-x.

Ray, D. K., N. D. Mueller, P. C. West, and J. A. Foley. 2013. "Yield Trends Are Insufficient to Double Global Crop Production by 2050." *PLoS ONE* 8: e66428. https://doi.org/10.1371/journal.pone.0066428.

Rice, B., and A. E. Lipka. 2019. "Evaluation of RR-BLUP Genomic Selection Models That Incorporate Peak Genome-Wide Association Study Signals in Maize and Sorghum." *Plant Genome* 12: 180052. https://doi.org/10.3835/plantgenome2018.07.0052.

Riedelsheimer, C., F. Technow, and A. E. Melchinger. 2012. "Comparison of Whole-Genome Prediction Models for Traits With Contrasting Genetic Architecture in a Diversity Panel of Maize Inbred Lines." *BMC Genomics* 13: 1–9. https://doi.org/10.1186/1471-2164-13-452.

Rutkoski, J., J. Benson, Y. Jia, G. Brown-Guedira, J. L. Jannink, and M. Sorrells. 2012. "Evaluation of Genomic Prediction Methods for Fusarium Head Blight Resistance in Wheat." *Plant Genome* 5: 51–61. https://doi.org/10.3835/plantgenome2012.02.0001.

Rutkoski, J. E., J. A. Poland, R. P. Singh, et al. 2014. "Genomic Selection for Quantitative Adult Plant Stem Rust Resistance in Wheat." *Plant Genome* 7: plantgenome2014-02. https://doi.org/10.3835/plantgenome2014.02.0006.

Savary, S., L. Willocquet, S. J. Pethybridge, P. Esker, N. McRoberts, and A. Nelson. 2019. "The Global Burden of Pathogens and Pests on Major Food Crops." *Nature Ecology & Evolution* 3: 430–439. https://doi.org/10.1038/s41559-018-0793-y.

Sehgal, D., U. Rosyara, S. Mondal, R. Singh, J. Poland, and S. Dreisigacker. 2020. "Incorporating Genome-Wide Association Mapping Results Into Genomic Prediction Models for Grain Yield and Yield Stability in CIMMYT Spring Bread Wheat." *Frontiers in Plant Science* 11: 197. https://doi.org/10.3389/fpls.2020.00197.

Shahinnia, F., M. Geyer, F. Schürmann, et al. 2022. "Genome-Wide Association Study and Genomic Prediction of Resistance to Stripe Rust in Current Central and Northern European Winter Wheat Germplasm." *Theoretical and Applied Genetics* 135: 3583–3595. https://doi.org/10.1007/s00122-022-04202-z.

Skinnes, H., K. Semagn, Y. Tarkegne, A. G. Marøy, and Å. Bjørnstad. 2010. "The Inheritance of Anther Extrusion in Hexaploid Wheat and Its Relationship to *Fusarium* Head Blight Resistance and Deoxynivalenol Content." *Plant Breeding* 129: 149–155. https://doi.org/10.1111/j.1439-0523.2009.01731.x.

Spindel, J., and H. Iwata. 2018. "Genomic Selection in Rice Breeding." In *Rice Genomics, Genetics and Breeding*, 473–496. Singapore: Springer. https://doi.org/10.1007/978-981-10-7461-5_24.

Spindel, J. E., H. Begum, D. Akdemir, et al. 2016. "Genome-Wide Prediction Models That Incorporate de Novo GWAS Are a Powerful New Tool for Tropical Rice Improvement." *Heredity* 116: 395–408. https://doi.org/10.1038/hdy.2015.113.

Sutton, J. C. 1982. "Epidemiology of Wheat Head Blight and Maize Ear Rot Caused by *Fusarium graminearum*." *Canadian Journal of Plant Pathology* 4: 195–209. https://doi.org/10.1080/07060668209501326.

Tan, B., and P. K. Ingvarsson. 2022. "Integrating Genome-Wide Association Mapping of Additive and Dominance Genetic Effects to Improve Genomic Prediction Accuracy in *Eucalyptus*." *Plant Genome* 15: e20208. https://doi.org/10.1002/tpg2.20208.

Veroneze, R., P. S. Lopes, M. S. Lopes, et al. 2016. "Accounting for Genetic Architecture in Single- and Multipopulation Genomic Prediction Using Weights From Genomewide Association Studies in Pigs." *Journal of Animal Breeding and Genetics* 133: 187–196. https://doi.org/10.1111/jbg.12202.

Zhang, W., K. Boyle, A. Brule-Babel, et al. 2021. "Evaluation of Genomic Prediction for Fusarium Head Blight Resistance With a Multi-Parental Population." *Biology* 10: 756. https://doi.org/10.3390/biology10080756.

Zhao, Y., M. Gowda, W. Liu, et al. 2012. "Accuracy of Genomic Selection in European Maize Elite Breeding Populations." *Theoretical and Applied Genetics* 124: 769–776. https://doi.org/10.1007/s00122-011-1745-y.

Zhong, S., J. C. M. Dekkers, R. L. Fernando, and J.-L. Jannink. 2009. "Factors Affecting Accuracy From Genomic Selection in Populations Derived From Multiple Inbred Lines: A Barley Case Study." *Genetics* 182: 355–364. https://doi.org/10.1534/genetics.108.098277.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.