1 **Sequential Post-Heading Applications for Controlling Wheat Blast: A Nine-Year**
2 **Summary of Fungicide Performance in Brazil**

3 João P. Ascari[1†], Jhonatan P. Barro[1†], Flávio M. Santana[2], José M.V. Padua[3], João L. N. Maciel[2],
4 Douglas Lau[2], Gisele A. M. Torres[2], Cheila C. Sbalcheiro[2], Claudine D. S. Seixas[4], Augusto C.
5 P. Goulart[5], Angelo A. B. Sussel[6], Carlos A. Schipanski[7], Débora F. Chagas[7], Maurício A. O.
6 Coelho[8], Tatiane D. N. Montecelli[9], Daniel R. Amaral[10], Adriano A. P. Custódio[11], Lucas S. O.
7 Moreira[11], Carlos M. Utiamada[12], Wilson S. Venâncio[13], Rita C. S. Goussain[14], Kaique S.
8 Alves[1], Emerson M. Del Ponte[1*]

9

10 [1] Departamento de Fitopatologia, Universidade Federal de Viçosa, Viçosa, 36570-900, MG, Brazil
11 [2] Embrapa Trigo, Passo Fundo, 99050-970, RS, Brazil
12 [3] Departamento de Agricultura, Universidade Federal de Lavras, Lavras, 37200-900, MG, Brazil
13 [4] Embrapa Soja, Londrina, 86001-970, PR, Brazil
14 [5] Embrapa Agropecuária Oeste, Dourados, 79804-970, MS, Brazil
15 [6] Embrapa Cerrados, Planaltina, 73310-970, DF, Brazil
16 [7] G12 Agro Pesquisa e Consultoria Agronômica, Guarapuava, 85015-344, PR, Brazil
17 [8] Empresa de Pesquisa Agropecuária de Minas Gerais, Patos de Minas, 38700-970, MG, Brazil
18 [9] Coodetec, Cascavel, 85818-650, PR, Brazil
19 [10] Instituto Federal do Triângulo Mineiro Uberaba, 38064-790, MG, Brazil
20 [11] Área de Proteção de Plantas, Instituto Agronômico do Paraná, Londrina, 86047-902, PR, Brazil
21 [12] Tagro, Londrina, 86070-460, PR, Brazil
22 [13] Estação Experimental Agrícola Campos Gerais, Palmeira, 84130-000, PR, Brazil
23 [14] Instituto Federal do Mato Grosso, Campo Verde, 78840-000, MT, Brazil
24

25 [†] These authors contributed equally
26 *Corresponding author: delponte@ufv.br

28 **Abstract**

29 Wheat blast, caused by *Pyricularia oryzae Triticum* (PoT) lineage, is a major constraint to wheat

30 production, mainly in the tropics of Brazil where severe epidemics have been more frequent. We

31 analyzed disease and wheat yield data from 42 uniform field trials conducted during nine years

32 (2012 to 2020) in order to assess whether the percent control and yield response were influenced

33 by fungicide type, region (tropical or subtropical), and year. Six treatments were selected, all

34 evaluated in at least 19 trials. Two fungicides were applied as solo active ingredients:

35 MANCozeb, and TEBUconazole, and four were premixes: AZOXystrobin + TEBU,

36 TriFLoXystrobin + PROThioconazole, TFLX + TEBU, and PYRAclostrobin + EPOXiconazole.

37 Percent control, calculated from back-transforming estimates by a meta-analysis network model

38 fitted to the log of the means, ranged from 43 to 58%, with all but PYRA + EPOX showing

39 efficacy greater than 52% on average, not differing among them. The variation in both efficacy

40 and yield response was explained by region and all but TEBU performed better in the subtropics

41 than in the tropics. Yield response from using three sequential sprays was around two times

42 greater in the subtropics (319 to 532 kg/ha) than in the tropics (149 to 241.3 kg/ha). No

43 significant decline in fungicide efficacy or yield response was observed in nine years of study for

44 any of the fungicides. Our results reinforce the need to improve control by adopting an integrated

45 management approach in the tropics given the poorer performance and lower profitability,

46 especially for the premixes, than in the subtropics.

47 **Keywords**: *Pyricularia oryzae*, chemical control, profitability, meta-analysis

48

49 **Introduction**

50   Wheat blast is caused by *Pyricularia oryzae Triticum* lineage (PoT, syn *Magnaporthe oryzae*,

51 MoT), an ascomycete fungus first found in 1985 in the state of Paraná, Brazil (Igarashi et al.

52 1986). Since then, wheat blast has spread to other wheat-growing countries in South America,

53 including Bolivia, Paraguay, Argentina, and Uruguay (Cruz and Valent 2017; Ceresini et al.

54 2018). About thirty years after its discovery, the global concern with wheat blast epidemics

55 increased significantly after its report in South Asia (Malaker et al. 2016), and East Africa

56 (Zambia) (Tembo et al. 2020).

57   The fungus infects both the leaves and the heads of the wheat plant, but infections that occur

58 during the reproductive stage are more frequent and of major economic significance; complete

59 bleaching of heads may occur, severely affecting grain filling (Cruz and Valent 2017; Ceresini et

60 al. 2018). Foliar infections are generally mild in wheat but may increase in severity, and
61 importance for head infections, when warm and wet weather prevails during the early season
62 (Cruz et al. 2016; Perelló et al. 2017). An early study reported a 27% reduction in yield due to
63 wheat blast (Goulart et al. 1990), but yield losses up to 70% may occur depending on the
64 infection timing, weather conditions, and cultivar susceptibility (Goulart and Paiva 2000).

65 Although the disease is present over a wide range of latitudes, the most severe epidemics have
66 been reported in wheat-growing regions in the tropics, during the summer/fall season sowings,
67 such as those in Central Brazil and Bolivia (Pagani et al. 2014; Cruz and Valent 2017), and more
68 recently, in Bangladesh (Islam et al. 2019). Because epidemics are favored by the occurrence of
69 temperatures between 25°C and 30°C, 10 hours or more of leaf wetness, and 24 to 48 hours of
70 relative humidity >90%, wheat blast epidemics are particularly more damaging in the tropics
71 than in the subtropics (Uddin et al. 2003; Cardoso et al. 2008; Silva et al. 2021).

72 Once the wheat blast pathogen is introduced, the necrotrophic fungus is capable of infecting
73 and surviving in other grasses nearby wheat fields which are assumed to serve as a source of
74 inoculum for epidemics in wheat if they are present prior to the wheat season (Tosa and Chuma
75 2014; Urashima et al. 2017; Ceresini et al. 2019). The ability of the fungus to disperse over long
76 distances is not entirely known but evidence has shown that *Pyricularia* spores can disperse
77 through air currents up to 1 km distant from the source (Urashima et al. 2007), or across
78 continents via infected seeds (Ceresini et al. 2018). Although several control methods have been
79 explored in research, including biological control agents (Chakraborty et al. 2020a, 2020b), the
80 combination of cultural (Coelho et al. 2016), nutritional (Xavier Filha et al. 2011; Silva et al.
81 2016), genetic, and chemical control have been commercially feasible and more effective in
82 disease management (Cruz et al. 2019; Cruppe et al. 2020).

83 Several chemicals have been evaluated for the control of the disease since the first blast
84 epidemics in Brazil (Goulart and Paiva 1993; Santana et al. 2013). These studies have shown that
85 two to three sequential applications of fungicides may be required for disease control, yet with
86 relatively modest levels of control being achieved (Santana et al. 2013). Currently, fifty-three
87 commercial fungicides have been registered for wheat blast control in Brazil (AGROFIT 2021).
88 These include Quinone outside Inhibitor (QoI) and Demethylation Inhibitor (DMI) marketed
89 solely or mixed together, but also multi-site mode of action fungicides such as mancozeb.

90 Despite the importance of wheat blast, the number of publications on chemical control of
91 wheat blast is relatively small and the results are inconsistent. Successful control with efficacy as
92 high as 90% has been achieved when combining the use of QoI + DMI premix and less
93 susceptible cultivar (Rios et al. 2016). However, levels as low as 45% efficacy have been

94   reported in susceptible cultivars grown at very favorable environments for blast outbreaks in the

95   Brazilian Cerrado (Pagani et al. 2014). In Bangladesh, 19-commercial fungicides had their

96   efficacy tested on a susceptible cultivar, and the blast control levels ranged from 43 to 96% (Roy

97   et al. 2020). A 23-environment fungicide trial conducted in Brazil and Bolivia reported various

98   levels of efficacy for QoI, DMI, and multi-site fungicides depending on disease pressure (Cruz et

99   al. 2019).

100   Meta-analytic approaches have become standard to summarize the effect of treatments for

101   fungicide testing data, including wheat diseases (Paul et al. 2008, 2018a; Machado et al. 2017;

102   Barro et al. 2019, 2020). Uniform fungicide trials targeting wheat blast control were established

103   in 2011 and performed yearly following a standardized protocol. The main goal of the network is

104   to gather information on disease control and yield loss prevention across the main growing

105   regions. The data have been analyzed and published as technical reports (Santana *et al.*, 2014;

106   2016a; 2016b; 2019a; 2019b; 2020a; 2020b). Data from the first three years of the cooperative

107   trials have been published in combination with Bolivian data (Cruz et al. 2019), but several

108   questions remained, including those related to differences between regions, years and

109   profitability of fungicide applications. Using data collected from an additional six-year period,

110   totaling 26 new trials, our objectives were to: 1) obtain meta-analytic estimates of wheat head

111   blast control efficacy and yield response; 2) evaluate whether the estimates vary over years,

112   regions, and on different levels of disease or yield; and 3) calculate fungicide profitability based

113   on the break-even probabilities.

114

115   **Material and Methods**

116   **Data source.** Data were obtained from 44 field trials conducted by researchers of the wheat

117   blast cooperative fungicide trial network (Rede de Ensaios Cooperativos de Brusone do Trigo)

118   during nine years (seasons) (2012 to 2020). The data have been published primarily in yearly

119   single reports for ranking fungicide efficacy (Santana et al. 2013, 2014, 2016a, 2016b, 2016c,

120   2019a, 2019b, 2020a, 2020b). Data from the 2020 season has not been published.

121   The trials were conducted in eleven municipalities across six Brazilian States: Paraná (PR),

122   São Paulo (SP), Distrito Federal (DF), Mato Grosso (MT), Mato Grosso do Sul (MS), and Minas

123   Gerais (MG) (Fig. 1). The trials were grouped into two climatic regions: Tropical (19 trials [DF,

124   MT, MS, MG]) and Subtropical (25 trials [PR, SP]).

125

126   **Experimental procedures.** A susceptible variety, adapted for the respective region, was used

127   in the trials (data not shown), and all agronomic practices (fertilization, weeds, and pest control)

128   were performed according to regional recommendations (Comissão Brasileira de Pesquisa de

129   Trigo e Triticale 2020). The trials were conducted following a completely randomized block

130   design with four replications (a plot of 12 m^2 was a replication). All fungicides were applied

131   three times, starting at the heading stage (60 of Zadoks growth stages) (Zadoks et al. 1974), and

132   following 7 to 10 days apart. A backpack sprayer pressurized by CO_2 calibrated to spray 200

133   L/ha was used to perform the applications.

134

135   **Wheat blast and grain yield assessments.** Head blast incidence (INC) (proportion of

136   diseased head) and conditional severity (SEV) (proportion of diseased spikelets in the diseased

137   head) (Maciel et al. 2013) were visually assessed in 1-m of each of the two central rows, at

138   wheat grain soft dough stage (85 of Zadoks growth stages) (Zadoks et al. 1974). Wheat blast

139   index (WBI) was calculated as WBI = (INC*SEV)/100. Yield was obtained by harvesting the

140   central rows (4 m^2) at full maturity. Grain weight and moisture were obtained for each treatment

141   plot (fungicide + untreated). Crop yield was expressed in kg/ha at 13% moisture.

142

143   **Fungicide treatment selection.** To be included in the analysis, a fungicide treatment should

144   have been tested in at least 19 trials conducted in at least four years and compared with an

145   untreated check in the same trial. Six fungicides met the criteria, including four DMI + QoI

146   premixes, and two single active ingredients (Table 1). After treatment selection, WBI and grain

147   yield data were available in 42 trials each.

148

149   **Network meta-analysis and inconsistency.** The data were available at the plot level for all

150   treatments for each variable of interest (WBI and grain yield). These were aggregated at the trial

151   level, which is a typical approach used in the meta-analysis (Madden et al. 2016). We fitted an

152   arm-based network model, also known as a two-way unconditional linear mixed model, directly

153   to the treatment means (log-transformed or untransformed) to further obtain control efficacy and

154   yield response (Paul et al. 2008; Machado et al. 2017). Given the statistical properties of the data

155   (Supplemental Fig. S1), means of WBI were log-transformed, while no transformation was

156   required to obtain the mean difference in grain yield. The arm-based model can be written as

157

158                            $$Y_i \sim N(\mu, \Sigma + S_i) \,,$$ (1)

159

160   where Y_i is the vector of L (log of the means of WBI) or absolute yield (D) for the six treatments

161   plus the untreated check for the ith study, μ is a vector representing the mean of Y_i across all

162   studies, Σ is a 7 x 7 between-study variance-covariance matrix (for the six treatments plus the

163   untreated check), and S_i is a within-study variance-covariance matrix for the ith study. N

164   indicates a multivariate normal distribution.

165   For this approach, a measure of within-study variability is required to weight studies based on

166   the inverse function of the sampling variance (Paul et al. 2008, 2010). Given the availability of

167   data at the plot level, the within-study variability of L and D was calculated from the mean

168   square error (MSE) obtained from a linear mixed model fitted to each individual trial, as

169   described (Machado et al. 2017). Maximum likelihood estimation models were fitted to the data

170   using the *rma.mv* function of *metafor* package (Viechtbauer 2010) of R (R Core Team 2021).

171   The yield response ($\overline{D}$) was calculated directly after model fitting by subtracting estimated

172   means of fungicide treatment and untreated check (Madden et al. 2016). For percent wheat blast

173   control ($\overline{C}$), we calculated the differences of the estimated means of the logs ($\overline{L}_{IND}$) which equals

174   the ratio of the two means (Paul et al. 2008). The $\overline{C}$ values and their 95% confidence intervals

175   (CIs) were obtained by back-transforming $\overline{L}_{IND}$ and the respective upper and lower limits of their

176   95% CIs as described in Equation 2.

177

178
$$\overline{C} = (1 - \exp(\overline{L}_{IND})) x\ 100 \qquad (2)$$

179

180   Network inconsistency, or the extent to which different sources of evidence are compatible, is

181   an important component to assess when performing a multi-arm network meta-analysis (Higgins

182   et al. 2012). The most important source is a design-by-treatment interaction, also known as

183   "design inconsistency", which provides a useful general framework for investigating

184   inconsistency (Piepho 2014; Madden et al. 2016). To test for network inconsistency, we used a

185   factorial-type ANOVA model to determine the significance of the *treatment* x *design* interaction,

186   evaluated based on the Wald test statistic. The null hypothesis suggests that the network is

187   consistent (Piepho 2014; Madden et al. 2016). Eight different designs (here design refers to the

188   set of fungicide treatments in the trial) were found in the trials reporting both WBI and yield

189   response (Supplemental Table S1).

190

191   **Moderator effects.** Categorical or continuous moderator variables that could explain, at least
192   a portion of the heterogeneity of the effects across trials, were included in the network model
193   (Equation 1) (Madden et al. 2016). The expanded model is given by

194
195 $$Y_i \sim N(\mu + \delta_i, \Sigma + S_i) \,, \tag{3}$$

196

197   where δ_i is the vector representing the moderator variable effect for the *i*th study (Paul et al.
198   2010). All other terms were defined previously at Equation 1.
199   As categorical, we created baselines for WBI and wheat grain yield based on the median of
200   the mean values in the untreated check. For baseline disease index, the trials were divided into
201   two groups, representing WBI_low (WBI＜10%) and WBI_high (WBI ≥10%) disease scenarios.
202   The baseline yield was defined as YLD_low (＜1200 kg/ha) or YLD_high (≥1200 kg/ha) based
203   on the median yield in the untreated check plot. Finally, we created an additional categorical
204   variable based on climatic region where trials were grouped into Tropical (DF, MT, MS, MG)
205   and Subtropical (PR, SP) regions as mentioned previously (Fig. 1). As continuous moderators,
206   year was included in the model to check whether there was any trend of decline in fungicide
207   efficacy or yield response over time (Dalla Lana et al. 2018).
208   The moderator variables included in the model were tested using a Wald-type chi-square test
209   to determine if their inclusion directly affected the differences in logs of WBI and the
210   untransformed yield values (Paul et al. 2008).
211

212   **Economic analysis.** Monte Carlo simulations were used to produce distributions of profits

213   that each fungicide would have in each region (Subtropical and Tropical) based on their

214   respective yield return (D, kg/ha). The profit was calculated from the difference between the

215   income (I, US\$/ha) and spraying cost (US\$/ha), where I is the product of D and the wheat price

216   (P, US\$/kg). D was assumed to follow a truncated normal distribution between 0 and $+\infty$, $D \sim$

217    $TN(\mu_D, \sigma_D)$, where μ_D is the mean D given by the estimated yield return ($\overline{D}$), and the σ_D is the

218   standard deviation which was given by standard error of ($\overline{D}$), i.e. $SE(\overline{D})$. P was assumed to

219   follow a Gamma distribution, $P \sim Gamma(\alpha, \beta)$, where α and β are the shape and the rate

220   parameters, respectively. To estimate these parameters, we gathered wheat price historical data

221   from the AGROLINK database from January 2012 to May 2021 (AGROLINK 2021). Two

222   methods were used to estimate the parameters: nonlinear regression using least-squares to fit the

223   empirical cumulative distribution function to the gamma cumulative distribution function, and

224   maximum likelihood estimation (MLE). We used a two-sample Kolmogorov-Smirnov test (KS-

225   test) to evaluate the best estimates, in which the parameters that produce distribution with higher

226   *P-value* in the KS-test against the empirical cumulative distribution.

227   The overall fungicide spraying cost (x) accounting for fungicide price of 2019/20 crop season,

228   and operational cost of 10 U\$/application for three applications are described in Table 1. The

229   spraying cost (S_C) was assumed to follow be uniformly distributed with values varying from 5%

230   above and below the overall fungicide spraying cost (x), therefore, $S_C \sim Unif(0.95x, 1.05x)$.

231   We ran a total of 50,000 Monte Carlo simulations for each variable (P, D, and S_C), the

232   distribution of I was obtained and then the distribution of profits was derived. Break-even

233   probabilities were calculated as the relative frequency of values that the income was equal to or

234   higher than the fungicide spraying cost ($I \geq C$).

235

236   **Results**

237   **Wheat blast index (WBI) and yield data at the trial level.** There was considerable variation

238   in WBI and grain yield in the untreated plots across seasons, regions, and locations/trials (each

239   point in Fig. 2 represents a single trial). WBI in the untreated plots of the trials ranged from 0 to

240   100% (median 11.06%). The median WBI was higher (12.3%) in the Tropical than in the

241   Subtropical (8.1%) region (Fig. 2 B). Across growing seasons, the highest (89.8%) and the

242   lowest (0.8%) WBI medians in the untreated check were recorded in the 2019 and 2017 seasons,

243   respectively (Fig. 2 C).

244   Baseline yield ranged from 15.6 to 4,276.2 kg/ha (median = 1,203.5 kg/ha) across the trials.

245   The median yield was lower in the Tropical (1,000 kg/ha) than in the Subtropical region (1,281

246   kg/ha) (Fig. 2 E). The highest median yield (2,173 kg/ha) was observed in 2014 and the lowest

247   (571.6 kg/ha) in the 2019 crop season (Fig. 2 F). As expected, lower WBI and higher grain yield

248   was observed in the fungicide treatments compared with the untreated check (Fig. 2 A to 2 D).

249

250   **Overall meta-analytic estimates of control efficacy and yield response.** For all fungicides

251   tested in the meta-analytic model, the overall WBI log response ratio ($\overline{L}_{IND}$) differed ($P <$

252   0.0001) from the untreated CHECK (Supplemental Table S2). Overall estimates of percent

253   control efficacy ($\overline{C}$), obtained from back-transforming differences of the estimates of log of WBI

254   ($\overline{L}_{IND}$) between the fungicide-treated and untreated plots, ranging from 43.2% and 58.0%.

255   MANC, AZOX + TEBU, TFLX + PROT, TEBU, and TFLX + TEBU reduced WBI by at least

256   52% and did not differ significantly among them ($P > 0.12$) based on linear contrasts. PYRA +

257   EPOX was the least effective treatment (43.2%) and did not differ from TEBU (53.5%; $P = 0.07$)

258   and TFLX + TEBU (52.2%; $P = 0.06$) (Supplemental Table S2). The difference in percent

259   control efficacy between the most and least effective fungicide was 14.8 percent points (Table

260   2). The Wald test for the treatment x design interaction showed that the network was consistent

261   ($P = 0.70$).

262   Yield response ($\overline{D}$) was significantly higher ($P < 0.0001$) in all single a.i. and dual mixtures

263   compared with the untreated CHECK (Table S3). The mean estimates of $\overline{D}$ ranged from 181.15

264   kg/ha to 420.10 kg/ha. The two single a.i. treatments, MANC (420.10 kg/ha) and TEBU (319.46

265   kg/ha) provided the greatest yield response, and linear contrasts showed no difference between

266   them ($P = 0.065$). These were followed by AZOX + TEBU (301.48 kg/ha) and TFLX+PROT

267   (299.73 kg/ha), which were not different between them ($P = 0.90$), but differed from

268   TFLX+TEBU (245.34 kg/ha; $P < 0.0001$). All fungicides differed from PYRA + EPOX (181.15

269   kg/ha) with regards to yield response. The difference between the highest and lowest yield

270   response among the treatments was 238.95 kg/ha (Table 2, Table S3). The Wald test for the

271   treatment x design interaction showed that the network was inconsistent, meaning that results

272   were dependent on the design ($P = 0.01$).

273

274   **Effect of moderator variables.** The categories of WBI and wheat grain yield as baselines did

275   not affect WBI or yield ($P > 0.05$). Similarly, year did not affect wheat grain yield ($P = 0.26$) or

276   WBI ($P = 0.74$), suggesting no decline in fungicide efficacy or yield response over time.

277   Based on the Wald test ($P < 0.0001$), the expanded model including the categorical moderator

278   variable region differed statistically from the simpler model for both disease index and yield

279   response. The control efficacy in the Subtropical region was numerically higher compared to the

280   Tropical region for all treatments. A difference of at least 19.1 percent points in $\overline{C}$ between
281   regions was significant ($P < 0.05$) for three fungicides (PYRA + EPOX, TFLX + PROT and
282   MANC) (Table 2). Similarly, yield response from the use of fungicides was generally higher in
283   the Subtropical than in the Tropical region. There was a statistical difference in $\overline{D}$ between
284   regions for all fungicides, except TEBU ($P = 0.1836$). Significant differences in yield responses
285   between regions ranged from 200 to 291 kg/ha (Table 2).

286   In general, there was a similar pattern in the relationship between yield response and
287   fungicide efficacy among regions. The treatment leading to the greatest mean yield response in
288   both Tropical and Subtropical regions was MANC (Fig. 3). Similarly, MANC was the
289   numerically most effective treatment in reducing disease index in the Subtropical region. For the
290   Tropical region, TEBU and AZOX + TEBU exhibited a high control efficacy (~47%). Again,
291   PYRA + EPOX provided the least yield response in both Tropical and Subtropical regions (Fig.
292   3).

293

294   **Profits and break-even probabilities.** Estimates of parameters of the Gamma distribution for
295   the distribution of wheat prices for the 2012 to 2020 period that produced higher *P*-value in the
296   KS-test were obtained using non-linear regression ($P = 0.9375$). The *P*-value in the KS-test for
297   the parameters estimated using MLE was 0.11. The estimates of the shape ($\boldsymbol{\alpha}$) and the rate ($\boldsymbol{\beta}$)
298   parameters were 19.4 and 0.54, respectively.

299   Overall, fungicides were more profitable in the subtropical region, with break-even
300   probabilities, $P(I \geq C)$, values higher than 0.99 for all fungicides (Fig. 4). In this region, the most
301   profitable fungicide was MANC, with a mean profit of US$269.73/ha. The least profitable
302   fungicide in the subtropical region was PYRA+EPOX, with a mean profit of US$118.17/ha. In
303   the tropical region, break-even probabilities of fungicides were much lower than those obtained
304   in the subtropics. The $P(I \geq C)$ values ranged from 0.17 (PYRA+EPOX) to 0.97 (MANC) (Fig.
305   4). The most profitable fungicide was again MANC, with a mean profit of US$95.00/ha and the
306   least profitable was PYRA+EPOX, with a negative mean profit of -US$17.66/ha.

307

308   **Discussion**
309   This study provides an updated summary of the effects of different fungicides applied
310   sequentially (three sprays starting at the heading stage) for managing wheat blast. For such, we
311   gathered data from 44 uniform field trials conducted during nine growing seasons (2012 to 2020)
312   across several wheat-producing states in Brazil. A previous study used a portion of the data used
313   in this work; 17 cooperative trials conducted from 2012 to 2014 in Brazil) also with the goal of

314 comparing fungicide treatments (Cruz et al. 2019). The present study differs from the previous

315 by evaluating a larger set of fungicide treatments, testing the effect of year and region within

316 Brazil, and performing an economic analysis (Cruz et al. 2019). Results of our analysis generally

317 corroborate the findings of that study for the Brazilian trials, which also reported a similar

318 performance among the QoI+DMI premixes and a protectant fungicide. Similarly, a recent single

319 field experiment (2019/20 season) conducted in Bangladesh reported a relatively high efficacy

320 (65%) for MANC, which was close to our upper limit (95% confidence interval) estimate (Roy

321 et al. 2020). The grain yield response from using MANC in the Bangladeshi study (744 kg/ha)

322 was within the expected gain (close to the upper limit) of estimated trials conducted in the

323 Subtropical region of Brazil. Among several differences in experimental conditions, it is worth

324 noting the difference in the concentration of MANC that was a bit higher (800 g/kg) in that study

325 compared with the recommended dose used in the Brazilian experiments (750 g/kg), which may

326 explain the higher levels of efficacy and yield response.

327 Commercial premixes of QoI+DMI have been tested more extensively than MANC in

328 independent research. For instance, in the study conducted by Cruz et al. (2019), the authors

329 reported a relatively high control efficacy (58 to 68%) for picoxystrobin + cyproconazole,

330 trifloxystrobin + tebuconazole, azoxystrobin + cyproconazole and pyraclostrobin +

331 epoxiconazole applied twice across six field trials conducted in Bolivia from 2014 to 2015.

332 Average yield responses obtained from applying those premixes in that study were extremely

333 high, in the magnitude of 1,834 kg/ha (Cruz et al. 2019).

334 In Brazil, contrary to our findings, replicated field studies have reported higher levels of

335 efficacy of PYRA+EPOX - ranging from 60% (Pagani et al. 2014) to 85% (Rios et al. 2016),

336 compared with our estimates (95% CI 31 to 52%) regardless of the region. Overall, we found

337 that this commercial premix performed the poorest among all treatments. Nevertheless, improved

338 efficacy similar to those obtained in Bolivia, using PYRA + EPOX, can be expected especially in

339 the southern region of Brazil, but with a high level of uncertainty (95% CI 17 to 74%).

340 Tebuconazole is an affordable option widely used by Brazilian growers not only for

341 controlling wheat blast, but also for managing other important wheat diseases such as Fusarium

342 head blight disease (Machado et al. 2017; Duffeck et al. 2020; Barro et al. 2020). The mean

343 estimates of TEBU applied solo (54%) as well as the premix TFLX + TEBU (52%) reported in

344 our meta-analysis were very similar to a two-year study (TEBU = 57%; TFLX + TEBU = 50%)

345 conducted in Midwest of Brazil during 2010 and 2011 crop seasons (Pagani et al. 2014).

346 Moreover, the yield responses from using the TEBU based fungicides reported in that study

347 (~400 kg/ha) (Pagani et al. 2014) were within the expected range, mainly for trials conducted in

348 the Subtropics where yield response was greater than in the Tropical region.

349   In general, the levels of control were superior and, on average, 18 percent points greater

350 in the Subtropical region (54 to 66%) compared with the Tropical region (24 to 47%). The only

351 exception was tebuconazole fungicide for which efficacy was not influenced by region. Our

352 findings demonstrated a similar levels of disease control reported in single studies conducted in

353 the tropics (60%) or Subtropics (85%) (Pagani et al. 2014; Rios et al. 2016).

354   Results of our profitability analysis using the means and respective uncertainty of the

355 estimates of yield return showed that, regardless of the region, the most profitable fungicide was

356 MANC, given its lower price, and similar efficacy and yield response compared with the

357 premixes. Although mancozeb was introduced in 1962, it is still important in the fungicide

358 market worldwide and known to be a cost-effective fungicide (Gullino et al. 2010; Thind and

359 Hollomon 2018). In fact, the probabilities of breaking even on costs of the commercial premixes

360 of fungicides were generally lower, especially in the Tropical region, for all premixes (which are

361 most costly) than MANC and TEBU, for which high break-even probabilities (> 92%) are

362 expected.

363   It is worth mentioning that there are two different wheat production systems in the tropics of

364 Brazil. The first is the irrigated and high-yielding system and where the blast is not a big concern

365 and the non-irrigated under which the trials were established. In the latter case, sowing dates

366 range from February to May (end of summer to begin of autumn) when the weather conditions

367 are favorable for the disease. The combination of less susceptible cultivars and fungicide

368 protection has been explored to improve disease management. For instance, Rios et al. (2016)

369 reported the effect of cultivar when using PYRA + EPOX with greatest control levels using a

370 cultivar that was considered less susceptible.

371   The use of premixes of single-site amended with multi-site fungicides has been tested more

372 recently for wheat blast control. Preliminary data from the uniform fungicide trials (Santana et

373 al. 2019b, 2019a, 2020a, 2020b) have shown grain yield benefits from adding a multi-site

374 fungicide (mancozeb) in the mixture and more data will become available in the near future to

375 confirm this observation. Additionally, the use of multi-site fungicides is important for managing

376 fungicide resistance (FRAC-BR 2021). In fact, less sensitive PoT populations to QoIs and DMIs

377 in Brazil have been reported, associated with mutations in cytochrome b gene (mainly G143A

378 substitution) (Castroagudín et al. 2015) or *CYP51* gene (several mutation points) (Dorigan et al.

379 2019; Poloni et al. 2021). However, using a relatively long time series we did not find evidence

380 of a decline in fungicide efficacy over the years for all commercial premixes amended with QoI

381   as well as TEBU applied solo. Whether QoIs are less effective or losing efficacy over the years

382   could not be inferred given that none of the fungicides had QoI as a sole active ingredient. If that

383   happens to be true, and confirmed by field research, it is possible that the DMI component in the

384   premix is responsible for the disease reduction. Further research in this area will be important to

385   contribute to the debate around the risk associated with the use of strobilurins for wheat blast

386   control (Castroagudín et al. 2015; Oliveira et al. 2015; Poloni et al. 2021).

387   In conclusion, the definition of the best options in fungicide programs for managing wheat

388   blast should take into account region-specific factors that affect the performance of fungicides

389   and also the need to extend control for other wheat diseases, a case where QoI + DMI premixes

390   have found use not only in Brazil but elsewhere (Blandino et al. 2006; Willyerd et al. 2012;

391   Barro et al. 2017; Paul et al. 2018b). Management tactics such as application of site-specific

392   fungicides amended with multi-site fungicides programs; use of locally-adapted wheat cultivars

393   carrying resistance genes against blast; and shifts in sowing time to escape conducive blast

394   weather at heading stage, especially in the tropics, should be considered in an integrated

395   management strategy against wheat blast. Overall, this work confirms the profitability of some

396   site-specific and a multi-site fungicide, report their efficacy, and yield return by controlling

397   wheat blast in both high disease-conducive region (tropical) and moderately disease-conducive

398   region (subtropical) to blast occurrence, which may be useful for decision-making when defining

399   fungicide programs.

400

409

410   **Data availability statement**

411   The data and R scripts that support the findings of this study are openly available in the Open

412   Science Framework project at osf.io/y7sgd/. A website was generated to better visualize the

413   scripts where all data and analyses are documented and reproducible (git.io/JGVCM).

414

415 **Author's contribution**

416   JPA and JPB contributed equally to this study. JPA, JPB and EMD conceived the idea,

417 analyzed the data and wrote the manuscript. KSA analyzed the data and wrote the manuscript.

418 FMS planned and coordinated the experiments; JMVP, JLNM, DL, GAMT, CCS, CDSS, ACPG,

419 AABS, CAS, DFC, MAOC, TDNM, DRA, AAPC, LSOM, CMU, WV, and RCSG conducted

420 the field trials and shared the data. All authors provided feedback and approved the final

421 manuscript.

422

423 **Conflict of interests**

424   The authors declare that they have no conflict of interests.

425

426 **Literature Cited**

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640 **Table 1.** Fungicide treatments evaluated for controlling wheat blast in 44 independent field trials

641 conducted across six Brazilian states (PR, SP, DF, MT, MS, and MG) from 2012 to 2020

Fungicide a.i.[a]	Chemical group[b]	Brand name	Nº trials	Dosage (mL or g/ha)	Cost[d] (US$/ha)
AZOX+TEBU	QoI+DMI	Azimut	28	750	73
MANC	DTC	Unizeb Gold	41	3,000	50
PYRA+EPOX	QoI+DMI	Opera	28	500	45
TEBU	DMI	Tebuco Nortox	19	500	52
TFLX+PROT	QoI+DMI	Fox	44	500	82
TFLX+TEBU	QoI+DMI	Nativo[c]	44	750	75

642 [a] a.i. (active ingredient); AZOX + TEBU = azoxystrobin + tebuconazole; MANC = mancozeb; PYRA + EPOX =

643 pyraclostrobin + epoxiconazole; TEBU = tebuconazole; TFLX + PROT = trifloxystrobin + prothioconazole; TFLX

644 + TEBU = trifloxystrobin + tebuconazole.

645 [b] QoI = Quinone-outside inhibitors; DMI = Sterol demethylation inhibitor; DTC = Dithiocarbamate.

646 [c] Included in all trials as positive control to wheat blast.

647 [D] Overall costs (US$/ha) considering commercial prices of the 2019/20 crop season and three applications

648 (operational cost for each application used was US$10.00/ha).

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651   **Table 2.** Overall means of Wheat Blast control efficacy ($\overline{C}$) and wheat yield response ($\overline{D}$) for each

652   fungicide treatment, relative to the untreated check, not conditioned (Overall) and conditioned

653   (moderator analysis) to two climatic regions (Tropical [DF, MT, MS, MG] and Subtropical [PR,

654   SP]), conducted during nine years (2012-2020) across six Brazilian states

Fungicide[a]	Region	Control efficacy (%)					Yield return (Kg/ha)				
		k[b]	$\overline{C}$	CI_L[c]	CI_U[c]	*P-value*[d]	k[b]	$\overline{D}$	CI_L[c]	CI_U[c]	*P-value*[d]
MANC	Overall	33	58.0	49.8	64.8		35	420.1	315.6	524.6	
	Tropical	13	42.1	26.1	54.7		14	241.3	94.7	387.9	
	Subtropical	20	66.5	40.6	81.1	0.0011	21	532.1	195.3	868.9	0.0027
TFLX + PROT	Overall	39	53.9	44.6	61.6		42	299.7	221.9	377.5	
	Tropical	15	40.8	22.9	54.5		17	149.3	44.7	254.0	
	Subtropical	24	59.9	26.4	78.2	0.0262	25	396.5	154.5	638.4	0.0004
TEBU	Overall	18	53.6	43.2	62.1		19	319.5	221.6	417.3	
	Tropical	8	47.2	28.2	61.1		9	209.0	52.7	365.3	
	Subtropical	10	56.9	13.3	78.6	0.3076	10	351.1	-14.6	716.8	0.1836
AZOX + TEBU	Overall	18	54.8	43.5	63.9		19	301.5	215.7	387.2	
	Tropical	7	47.1	26.2	62.1		8	157.0	52.7	261.3	
	Subtropical	11	58.4	10.9	80.6	0.2704	11	410.3	162.2	658.4	0.0006
TFLX + TEBU	Overall	39	52.2	43.5	59.6		42	245.3	172.9	317.8	
	Tropical	15	42.4	26.1	55.2		17	123.9	25.7	222.1	
	Subtropical	24	57.4	24.3	76.0	0.0685	25	323.4	94.6	552.2	0.0028
PYRA + EPOX	Overall	19	43.2	31.8	52.8		22	181.1	114.8	247.5	
	Tropical	8	24.2	2.81	40.9		10	29.1	-49.8	108.1	
	Subtropical	11	54.3	17.5	74.7	0.0037	12	255.0	65.4	444.6	<0.0001

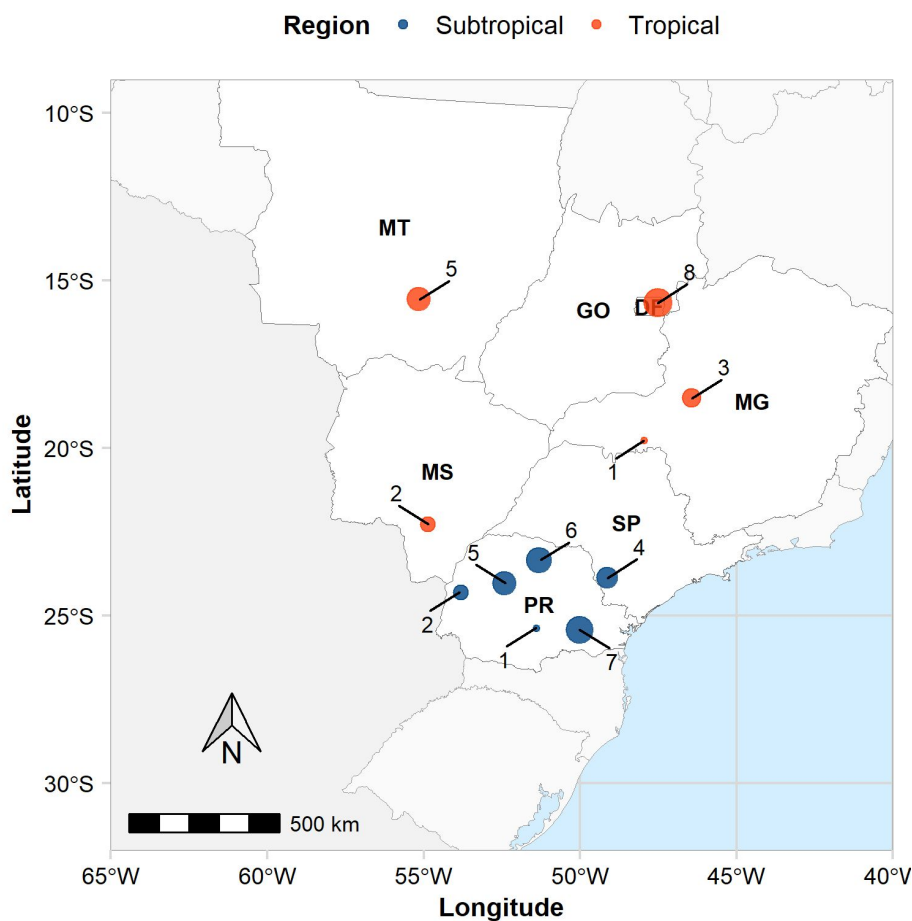655   [a] See Table 1 for complete information on the fungicides.

656   [b] number of trials that each fungicide was evaluated.

657   [c] upper (CI_U) and lower (CI_L) limits of the 95% confidence interval around $\overline{C}$ and $\overline{D}$.

658   [d] probability value (significance level) for the effect of fungicide on disease reduction and yield response (at the selected

659   climatic regions).

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Fig. 1. Geolocation of eleven municipalities across six Brazilian states where 44 fungicide trials were conducted from 2012 to 2020 (Campo Mourão - PR, Guarapuava - PR, Campo Verde - MT, Dourados - MS, Itaberá - SP, Londrina - PR, Palmeira - PR, Palotina - PR, Patos de Minas - MG, Planaltina - DF, Uberaba - MG). Dots were colored by climatic region and the size of the circle is proportional to the number of trials conducted at each location.

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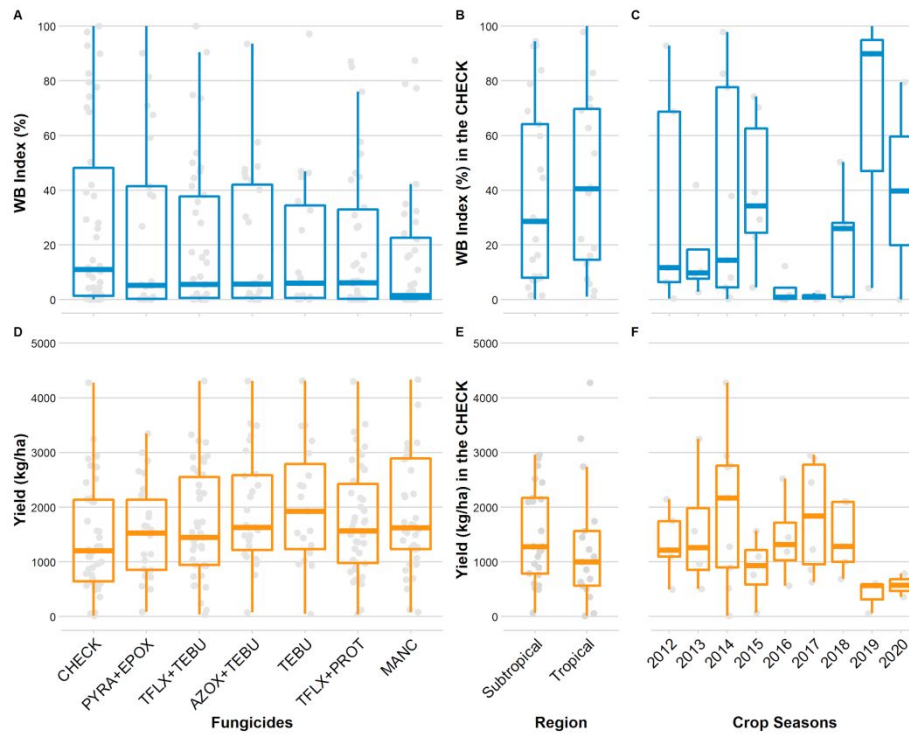
Fig. 2. Box plots depicting the means of wheat blast index (%) and wheat grain yield (kg/ha)

671 (across years and locations) of the untreated (CHECK) and fungicide-treated plots (**A** to **D**); and

672 the means of the same variables in the untreated plots within-region (**B** to **E**) and within-year (**C**

673 to **F**) measured from a set of 44 field trials conducted from 2012 to 2020. Climatic regions

674 defined in this study were: Tropical (DF, MT, MS, MG) and Subtropical (PR, SP). The thick

675 horizontal line inside the box represents the median, the limits of the box represent the lower and

676 upper quartiles, and the circles represent the yearly means of each treatment. See Table 1 for

677 information on the fungicide treatments.

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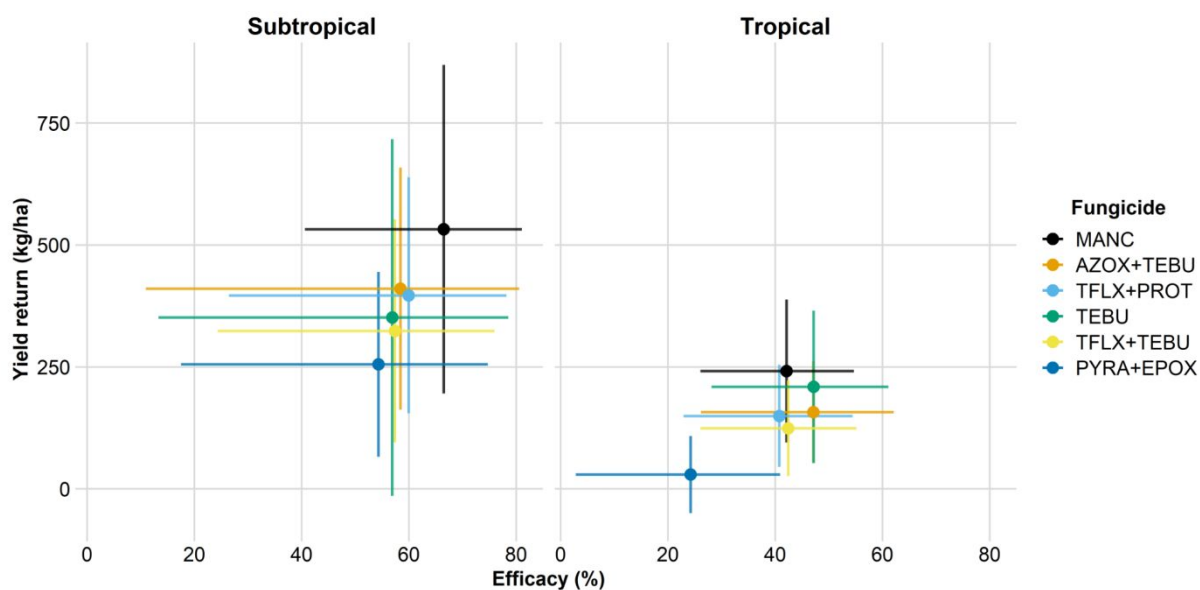
Fig. 3. Relationship between fungicide efficacy and wheat grain yield relative to the untreated check, for six selected fungicide treatments evaluated during nine years (2012 to 2020) across 44 field trials conducted across six Brazilian states (PR, SP, DF, MT, MS, and MG). Bars show the upper and lower limits of 95% confidence intervals around point estimates for both responses. See Table 1 for complete information on the evaluated fungicides.
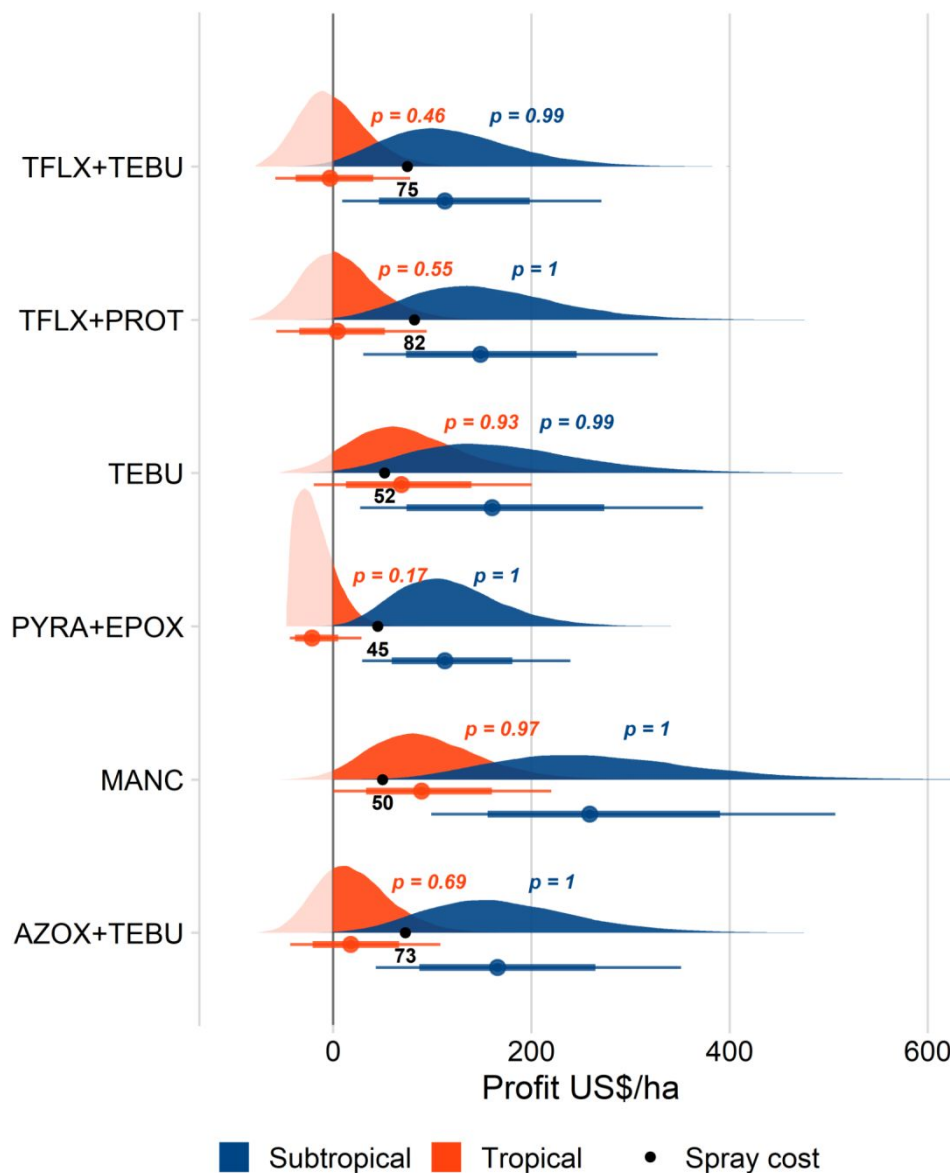
Fig. 4. Half-eye plots (density and point intervals) of profits (50,000 simulation runs) based on the meta-analytic estimate of yield return (kg/ha) for six fungicide treatments conditioned of two climatic regions (Tropical and Subtropical) evaluated during nine crop-seasons (2012 to 2020). The thinner error bars depict the 2.5 and 97.5 percentile of the distribution, while the thicker error bars represent 25 and 75 percentiles, and the solid colored point gives the median profit for each fungicide and region. p gives the break-even probabilities, i.e, income greater than the cost of each fungicide in each respective region. The numbered black dots represent the spraying costs in US$/ha of each fungicide.

1   **Sequential Post-Heading Applications for Controlling Wheat Blast: A Nine-Year**

2   **Summary of Fungicide Performance in Brazil**

3   **João P. Ascari et al.**

4   **Supplemental Figure and Tables**

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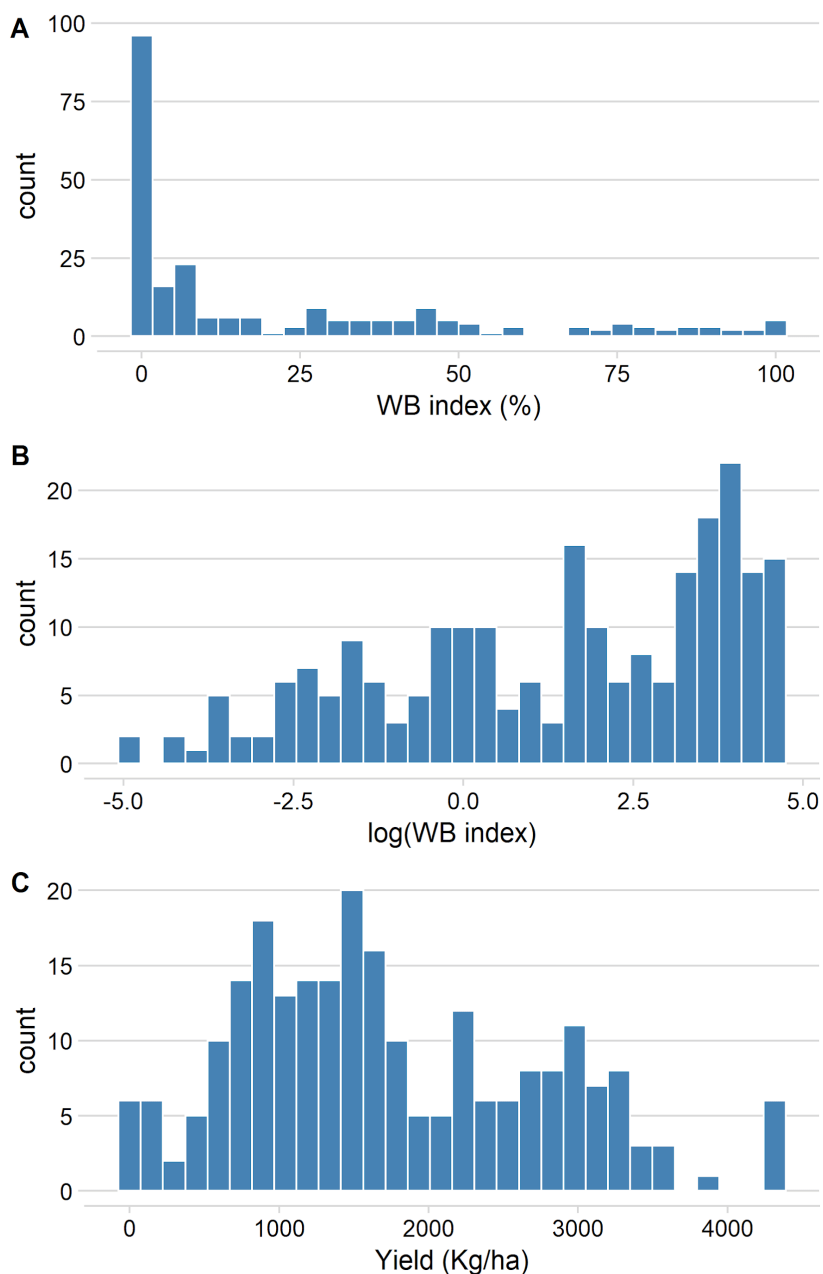
7   **Fig. S1**: Histograms for the distribution of Wheat blast index - WBI (**A**) and wheat grain yield
8   (**C**) to check normality; **B**: log-transformed WBI data for normalizing the distribution and use in
9   the meta-analysis models.
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Table S1. Designs (set of fungicide treatments by each trial) identified in 44 independent trials conducted from 2012 to 2020 in 11 municipalities across six Brazilian states (PR, SP, DF, MT, MS and MG).

Design	Fungicides a.i. + untreated check [a]	WB index[b]	Yield[b]
1	CHECK; AZOX+TEBU; MANC; PYRA+EPOX; TEBU; TFLX+PROT; TFLX+TEBU	4	4
2	CHECK; AZOX+TEBU; PYRA+EPOX; TEBU; TFLX+PROT; TFLX+TEBU	5	5
3	CHECK; AZOX+TEBU; MANC; TEBU; TFLX+PROT; TFLX+TEBU	8	9
4	CHECK; AZOX+TEBU; MANC; TFLX+PROT; TFLX+TEBU	1	1
5	CHECK; MANC; PYRA+EPOX; TFLX+PROT; TFLX+TEBU	10	13
6	CHECK; MANC; TEBU; TFLX+PROT; TFLX+TEBU	1	1
7	CHECK; MANC;; TFLX+PROT; TFLX+TEBU	9	7
8	CHECK; TFLX+PROT; TFLX+TEBU	1	2

[a] See Table 1 for complete information about the treatments;

[b] Number of trials that each design of treatments was identified for both WB index and yield.

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19 **Table S2.** Overall means and respective confidence intervals of log response ratio ($\overline{L}_{IND}$) and

20 calculated percent control ($\overline{C}$) of Wheat Blast (WB) relative to untreated check provided by six

21 fungicides evaluated during nine years (2012 to 2020) across 44 studies conducted in six Brazilian

22 states (PR, SP, DF, MT, MS and MG).

Fungicide[a]	k[b]	$\overline{L}_{IND}$	SE($\overline{L}$)	CI_L[c]	CI_U[c]	*P value*	$\overline{C}$	CI_L[c]	CI_U[c]
		Effect Size					**WB Control (%)**		
MANC	33	-0.8677	0.0904	-1.0449	-0.6905	<0.0001	58.00	49.86	64.82
AZOX + TEBU	18	-0.7946	0.1144	-1.0188	-0.5704	<0.0001	54.82	43.46	63.89
TFLX+PROT	39	-0.7745	0.0938	-0.9583	-0.5907	<0.0001	53.90	44.60	61.64
TEBU	18	-0.7678	0.1035	-0.9706	-0.5650	<0.0001	53.59	43.16	62.11
TFLX+TEBU	39	-0.7395	0.0854	-0.9068	-0.5722	<0.0001	52.26	43.56	59.61
PYRA+EPOX	19	-0.5669	0.0939	-0.7509	-0.3829	<0.0001	43.27	31.81	52.80

23 [a] See Table 1 for complete information of the evaluated fungicides;
24 [b] number of trials that each fungicide was evaluated;
25 [c] upper (CI_U) and lower (CI_L) limits of the 95% confidence interval around $\overline{L}_{IND}$ and $\overline{C}$.
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28 **Table S3**. Overall means and respective confidence intervals of unstandardized difference in wheat

29 grain yield ($\overline{D}$) between fungicide-treated and untreated plots, and percent yield increase ($\overline{Y}$) for six

30 selected fungicide treatments evaluated during nine years (2012 to 2020) across 44 studies conducted

31 in six Brazilian states (PR, SP, DF, MT, MS and MG).

Fungicide[a]	k[b]	Effect size					Yield Return (%)		
		$\overline{D}$	$SE(\overline{D})$	CI_L[c]	CI_U[c]	P value	$\overline{Y}$	CI_L[c]	CI_U[c]
MANC	35	420.10	53.30	315.62	524.57	<0.0001	47.55	32.25	64.62
TEBU	19	319.46	49.91	221.63	417.29	<0.0001	38.68	26.54	51.98
AZOX + TEBU	19	301.48	43.75	215.73	387.24	<0.0001	37.01	23.07	52.51
TFLX+PROT	42	299.73	39.69	221.92	377.53	<0.0001	32.42	21.84	43.93
TFLX+TEBU	42	245.34	36.98	172.85	317.83	<0.0001	29.08	19.13	39.86
PYRA+EPOX	22	181.15	33.85	114.79	247.50	<0.0001	23.76	14.62	33.64

32 [a] See Table 1 for complete information on the fungicides;
33 [b] number of trials that each fungicide was evaluated;
34 [c] upper (CI_U) and lower (CI_L) limits of the 95% confidence interval around $\overline{D}$ and $\overline{Y}$.