Fungicide resistance management

Femke van den Berg
Introduction

- Resistance management strategies should be based on evidence

- **Example statement:** “It is important to use the maximum dose permitted on the product label, in order to prevent, or at least slow down, the development of resistance.”
Are there governing principles?

Governing Principles Can Guide Fungicide-Resistance Management Tactics

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Abstract
Fungicide-resistance management would be more effective if principles governing the selection of resistant strains could be determined and validated. Such principles could then be used to predict whether a proposed change to a fungicide application program would decrease selection for resistant strains. In this review, we assess a governing principle that appears to have good predictive power. The principle states that reducing the product of the
Governing principles
Based on Milgroom & Fry (1988) and Staub & Sozzi (1983)

- The selection coefficient:
  \[ sT = (r_R - r_S)T \]

- Rate of increase of resistant strain
- Rate of increase of sensitive strain
- Exposure time

**Strategy 1:** Reduce both \( r_R \) and \( r_S \)
**Strategy 2:** Reduce \( r_R \) relative to \( r_S \)
**Strategy 3:** Reduce exposure time
Tactics investigated

- **b**: Adjust dose per spray
- **c**: Adjust number of sprays
- **d**: Adjust total dose of the spray program
- **g**: Adjust timing
- **e**: Add a fungicide, B
- **f**: Mix, Alternate
- **a**: Split dose
### Success of tactics summary

<table>
<thead>
<tr>
<th></th>
<th>increase</th>
<th>No effect</th>
<th>decrease</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Increase dose</td>
<td>16</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>T2</td>
<td>Increase spray number</td>
<td>6</td>
<td>0</td>
<td>0</td>
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<tr>
<td>T5</td>
<td>Split the dose</td>
<td>10</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>T3</td>
<td>Mix: add a fungicide</td>
<td>1</td>
<td>6</td>
<td>46</td>
</tr>
<tr>
<td>T4</td>
<td>Alternate</td>
<td>1</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>T6</td>
<td>Adjust spray timing</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

\[ sT = (r_R - r_S)T \]
Adding a mixing partner: strategy 1

- \( sT = (r_R - r_S)T \)
- A mixing partner affects \( r_R \) and \( r_S \) in the same way
- Strategy 1 applies: reduce both \( r_R \) and \( r_S \)

<table>
<thead>
<tr>
<th>Adding a mixing partner .......... selection</th>
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<tbody>
<tr>
<td>increase</td>
</tr>
<tr>
<td>Multi-site</td>
</tr>
<tr>
<td>Single-site</td>
</tr>
</tbody>
</table>

- General conclusion: as expected adding a mixing partner reduces selection for resistance
Adding a mixing partner – further details

Phytopathology REVIEW

Mixtures as a Fungicide Resistance Management Tactic

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ABSTRACT

The effect of dose: strategy 2

- \( sT = (r_R - r_S)T \)
- An increased dose reduces \( r_S \) more strongly than \( r_R \)

<table>
<thead>
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<th>Increased dose .......... selection</th>
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</thead>
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<tr>
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<td>decrease</td>
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</tr>
<tr>
<td>experiments</td>
<td>16</td>
<td>1</td>
<td>2 (1)</td>
<td>19</td>
</tr>
<tr>
<td>models</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>8</td>
</tr>
</tbody>
</table>

- Contrary to general held opinion there is clear evidence that an increased dose increases selection
- Careful: we are not advocating to reduce dose as this may compromise effective control!
The effect of dose – further details

**REVIEW**

**The dose rate debate: does the risk of fungicide resistance increase or decrease with dose?**

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Number of applications: strategy 3

- $sT = (r_R - r_S)T$
- An increased number of applications increases the time-span over which selection acts

<table>
<thead>
<tr>
<th>Increase spray number</th>
<th>increase</th>
<th>No effect</th>
<th>decrease</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>6</td>
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</table>

- General conclusion: an increased number of spray applications increases selection
Practical resistance management tactics

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<tr>
<th></th>
<th>increase</th>
<th>no effect</th>
<th>decrease</th>
<th>total</th>
</tr>
</thead>
<tbody>
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<td>T7</td>
<td>Replace a spray</td>
<td>0</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>T8</td>
<td>Mix and reduce dose</td>
<td>1</td>
<td>5</td>
<td>17</td>
</tr>
<tr>
<td>T9</td>
<td>Alternate versus mixing</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
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Replace part of the sprays by sprays with another MOA
Add a mixing partner and reduce the dose of the high-risk fungicide.
Change the alternation into a mixture strategy with half dosages of the fungicides.
Summary

- Very simple governing principle can explain effect of fungicide resistance management tactics on selection for resistance in majority of cases
- 84% of published cases agree with prediction
- 5% of published cases contradict predictions
- Useful tool to inform decisions about fungicide resistance management when there is no time to wait for the accumulation of new evidence
Thank you for your attention!

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Introduction

- Combining field experiments and modelling
- Governing principle, qualitative
- Dynamic models, towards quantitative
- Guide field research on resistance management
- Results influence policy through FRAC, FRAG, CRD, EPPO
The heterozygote is partially sensitive.

At low frequency R genes are, due to sexual reproduction, mainly in heterozygotes.

Most plant pathogens are haploid at time when fungicide is applied, or are clonal.

Reasoning of insecticide resistance does not apply.
Fungicide dose, missing evidence

- Mechanisms by which an increased dose may reduce resistance risk
  - Stress induced mutation
  - Mutation limitation (emergence)
  - Refugia
  - Converging dose-response curves
  - Partial resistance/multi-gene resistance

- These mechanisms are hypothetical, none have been shown to apply

- Virtually all available evidence suggests that increasing fungicide dose increases selection for resistance
The effect of Dose.

**Mutation limitation and emergence**

**Low dose**

**High dose**

**Mutation**

**Invasion**
Fungicide dose, missing evidence

- Converging dose-response curves

**Graph:**

- **Lolium rigidum**
- Sensitive and resistant curves
- Diclofop-methyl dose (g ha\(^{-1}\))

Neve & Powels (2005)
Adjust timing – protective vs curative

- **Strictly:**
  - Protectant: application prior to infection
  - Curative: application after infection

- **Brent and Hollomon (2007)**
  “to the authors knowledge there is no experimental evidence comparing the resistance risks of prophylactic versus threshold-based schedules, and research on this would be useful.”
Adjust timing – protective vs curative

\[ sT = (r_R - r_S) T \]

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<tbody>
<tr>
<td>adjust timing</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>6</td>
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</tbody>
</table>

- Protective use is in many cases essential for effective disease control
- There is no evidence that protective use is essential for resistance management