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Field and Forage Crops

A Meta-analysis and Economic Evaluation of Neonicotinoid Seed Treatments and Other Prophylactic Insecticides in Indiana Maize From 2000–2015 With IPM Recommendations

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Abstract

Corn rootworm remains the key pest of maize in the United States. It is managed largely by Bt corn hybrids, along with soil insecticides and neonicotinoid seed treatments (NSTs), the latter of which are applied to virtually all conventionally (non-Bt) produced maize. Frequently, more than one of these pest-management approaches is employed at the same time. To determine the utility and relative contributions of these various approaches, a meta-analysis was conducted on plant health and pest damage metrics from 15 yr of insecticide efficacy trials conducted on Indiana maize to compare the pest-protection potential of NSTs to that of other insecticides and Bt hybrids. The probability of recovering the insecticide cost associated with each treatment was also calculated when possible. With the exception of early-season plant health (stand counts), in which the NSTs performed better than all other insecticides, the vast majority of insecticides performed similarly in all plant health metrics, including yield. Furthermore, all tested insecticides (including NSTs) reported a high probability (>80%) of recovering treatment costs. Given the similarity in performance and probability of recovering treatment costs, we suggest NSTs be optional for producers, so that they can be incorporated into an insecticide rotation when managing for corn rootworm, the primary Indiana corn pest. This approach could simultaneously reduce costs to growers, lower the likelihood of nontarget effects, and reduce the risk of pests evolving resistance to the neonicotinoid insecticides.

Key words: Neonicotinoid seed treatment, insecticide efficacy, corn rootworm

Insecticide use is key component of crop protection in many commodities with pesticide use in general becoming the dominant approach to U.S. pest control following WWII (Osteen 2003). This is in part due to a combination of low cost, effectiveness, and convenience or ease of application (MacIntyre 1987). However, insecticide use is not without some significant drawbacks, both ecological and economical. While the definition of Integrated Pest Management (IPM) has evolved over the past 50+ yr (Kogan 1998), an ideal modern IPM program would include monitoring and management of key pests (including weeds, insects, and fungal pathogens), use of multiple suppressive tactics to achieve economic levels of control, and the judicious use of pesticides where necessary as determined by economic thresholds (Ehler 2006). In reality, modern IPM in field crops such as maize and soybeans frequently falls short of this ideal, relying largely on prophylactic pesticide use to treat pests, with limited rotation of active ingredients (AIs) to mitigate resistance (Ehler 2006). By 2011, preemptive insecticide use increased to 34–44% in soybeans and 79–100% of maize in the United States while pest pressures have not increased over the same period (Douglas and Tooker 2015). While this approach may be partially dictated by current market efficiencies, it fails to address the root cause of pest problems (Ehler 2006). Despite this, the benefits of IPM have been well documented with a review covering 61 economic evaluations of IPM over a span of 20 yr (1973–1993) in eight commodity groups (cotton, soybeans, corn, vegetables and flowers, fruits, peanuts, tobacco, and alfalfa), finding a 14.9% decrease in pesticide use, 2.8% decrease in production cost, an 11.4% increase in yield, and a 47.8% net return per acre (Norton and Mullen 1994).

In the midwestern United States, a variety of IPM strategies have been researched and developed (Levine and Oloumi-Sadeghi 1991) to deal with the primary pest of maize, the corn rootworm (CRW) (*Diabrotica virgifera* LeConte and *D. barberi* Smith & Lawrence) (Coleoptera: Chrysomelidae) (Gray et al. 2009). These include crop rotation (Levine and Oloumi-Sadeghi 1991), planting date alteration

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(Musick et al. 1980, Naranjo and Sawyer 1987), and varying tillage practices (Gray and Tollefson 1988a,b). An increase in rotation resistant CRW populations (Krysan et al. 1984, Onstad et al. 1999, Levine et al. 2002), pesticide resistance (Ball and Weekman 1963, Meinke et al. 1998, Wright et al. 2000), and resistance to Bt corn hybrids (Gassmann et al. 2011) have combined to reduce the effectiveness and applicability of these IPM strategies. Foliar sprays have occasionally been used within an IPM framework with action thresholds at 1–1.57 beetles/plant in continuous corn, and 0.83 beetles/plant in first year corn (Pruess et al. 1974, Godfrey and Turpin 1983). These foliar sprays target adult CRW in an effort to reduce larval damage in the subsequent season and protect plant silks from adult feeding. However, the efficacy of this approach is heavily influenced by abiotic factors that dictate pest phenology (Naranjo and Sawyer 1989), including precipitation (Mayo 1984), and is likely to be more expensive than a single soil applied insecticide at planting if more than two sprays are needed (Bergman 1987). Furthermore, the sampling methods (Foster et al. 1982, Steffey et al. 1982) designed to accurately count adult beetles and inform action thresholds (Pruess et al. 1974, Godfrey and Turpin 1983) are labor intensive and poor predictors of economic damage and yield loss in the next year (Hein and Tollefson 1985, Foster et al. 1986). This disconnect has been attributed to a lack of basic research examining CRW population dynamics and insect plant interactions (Hein et al. 1988). For the latter part of the 20th century, prophylactic application of soil insecticides was found to be the most economically feasible approach to CRW management in continuous corn due to the difficulty in predicting larval populations (Foster et al. 1986).

With the diminished utility of traditional IPM practices, logistical hurdles such as those outlined above, along with the economic uncertainties associated with conducting a consistent IPM program, CRW management in commercial maize production has continued to move toward a prophylactic, insurance-based approach, frequently using *Bt* hybrids as the cornerstone (Gray 2011). Hybrids utilizing *Bt* technology have largely controlled CRW since their initial introduction in 2004–2006 (Storer et al. 2006, Ma et al. 2009) although nonhigh dose toxins, variability of toxin expression in plant material, and inadequate refuges have led to several cases of field-evolved *Bt* resistance in CRW (Gassmann et al. 2011, Gassmann et al. 2014). The move away from traditional IPM approaches in maize and soy crops is further manifested by the introduction and rapid adoption of neonicotinoid seed treatments (NSTs). As of 2011, over 80% of maize and 34–44% of soy planted in the United States are treated with either clothianidin (CLO) or thiamethoxam as a seed treatment at application rates of 0.25–1.25 mg/kernel before sale to the grower (Krupke et al. 2012; Douglas and Tooker 2015). The sharp increase in NST use has not been in response to any increase in pest damage or threat (Douglas and Tooker 2015). This runs contrary to a key principle of IPM (Pedigo and Rice 2009), that prioritizes the judicious use of pesticides as a means forestalling resistance and limiting the likelihood of negative effects on both human and environmental health.

NSTs have been marketed as a highly versatile and effective insecticide group with relatively low risk to nontarget organisms in comparison with older insecticide classes (Jeschke and Nauen 2008). While the 1.25 mg/kernel rate of CLO is labeled for control of the Western CRW (*D. virgifera virgifera* LeConte), NSTs are also labeled for other early-season secondary pests attacking seeds and the developing root tissue (Jeschke et al. 2011) including wireworms (Riley and Keaster 1979), seedcorn maggots (Higley and Pedigo 1984), and white grubs (Jordan et al. 2012). Both seedcorn maggots and wireworms preferentially attack the seed region of young plants early in the season (Riley and Keaster 1979, Higley and Pedigo 1984) whereas white grubs and CRW attack the roots (Metcalf and Metcalf 1993)) causing plant lodging, reduced water uptake, and increasing potential for yield loss (Levine and Oloumi-Sadeghi 1991). The vast majority of these secondary pests are not relevant to most producers as economic infestations are erratic and difficult to predict (Royer et al. 2004), with the exception of seedcorn maggot infestations, which can be reliably anticipated based on the incorporation of a green cover crop (Hammond 1990). Recent research (Alford and Krupke 2017) indicates that the period when neonicotinoid residues are present within plant tissues offers a good fit with the phenology of some secondary pests, but does not align well with the phenology of the Western CRW, the primary insect pest of North American maize production.

While multiple reviews have addressed the nontarget effects of neonicotinoids on a range of organisms, including pollinators, migratory waterfowl, and aquatic invertebrates (Goulson 2013, Nuyttens et al. 2013, Godfray et al. 2014, Morrissey et al. 2015, Pisa et al. 2015), only one review has compared the crop protection potential of neonicotinoids against that of previous insecticide classes; this is surprising given the rapid adoption and widespread use of neonicotinoids in maize. Tinsley et al. (2015) utilized maize insecticide efficacy trial data from 2003 to 2014 from Illinois and Nebraska trials to describe the damage reduction attributable to various management strategies. Treatments included NSTs at the CRW rate (1.25 mg CLO per kernel), soil insecticides, single-toxin Bt maize (± soil insecticide), and dual-toxin Bt maize (± soil insecticide). The data were analyzed by pairing the node injury for each insecticidal treatment with that of the untreated control for each study location. A regression of that panel data was then used to create efficacy equations. Soil insecticides, including both granular and liquid formulations, were grouped together regardless of application rate or AI and included organophosphates, phenylpyrazoles, and pyrethroids. Bt hybrids were also treated with a low, ‘non-CRW,’ rate (0.25–0.50 mg ai per kernel) of NST. The dual-toxin Bt maize + a soil insecticide approach led to the greatest significant reduction in larval CRW damage (97%), while the NSTs led to smallest damage reduction (48%). Soil insecticides performed about as well as single toxin Bt alone with respective reductions of 72% and 78% suggesting single toxin Bt without a soil insecticide could be rotated with soil insecticides alone to extend the utility of both approaches. Another conclusion of Tinsley et al. (2015) was that CRW rates of NSTs (1.25 mg ai per kernel) are unlikely to provide adequate protection at higher CRW densities and their associated high-damage potential, compared with other available options.

The objective of our analysis is to compare NSTs to previously and currently utilized prophylactic soil insecticides to assess their overall effectiveness across multiple agronomic parameters in maize. Unlike Tinsley et al. (2015), soil insecticides were grouped by AI and application rate before analysis to estimate the value of products available in the maize insecticide market. Our data source is comprised of 15 yr (2000–2015) of insecticide efficacy trials in maize conducted by the Purdue entomology field crops lab. These trials were conducted annually to provide growers an unbiased source of efficacy for maize insecticides currently available to them. As the sample size, variance, and mean are known for each treatment, these data are readily analyzed within a meta-analytical framework, allowing us to compare the overall mean effect of each AI and rate. Finally, we calculated the probability of a grower financially recouping seed and insecticide costs for each insecticide/rate by using the overall insecticide associated yield increase and a range of current insecticide and maize sell prices. This analysis is spurred on by both the

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unprecedented use rates of NSTs in maize and the growing reports of *Bt* resistance among CRW populations at various locations throughout the corn belt. The results will allow us to explore and assess the most appropriate insecticide options for producers in regions with varying levels of CRW pressure and Bt resistance.

Materials and Methods

Source Data

Data sets comprising insecticide efficacy studies conducted yearly from 2000 to 2015 by the Purdue entomology field crops lab were used. These studies were carried out across five agricultural field stations in the State of Indiana, representing a cross-section of the regions where the majority of maize production in the state occurs: Pinney Purdue Agricultural Center at 41°26′35.22″N 86°55′48.34″W, the Northeast Purdue Agricultural Center at 41°6′15.43″N 85°23′55.67″W, Davis Purdue Agricultural Center at 40°15′12.07″N 85°8′52.92″W, Throckmorton Purdue Agricultural Center at 40°17′48.56″N 86°54′11.26″W, and Southeast Purdue Agricultural Center at 39°2′12.49″N 85°31′42.58″W. Trial plots were conducted in both large and small maize plot arrangements in a randomized complete block design with four blocks in all years. Large plot studies were conducted in years 2000–2007 with a given treatment consisting of three adjacent rows, 70.4–183 m in length depending on the year and location. Small plot trials were conducted in all years with a treatment consisting of a single row, 30.5 m in length. Both plot types were included in the meta-analysis. Of the 69 efficacy trials used in this project, soybean was used as the previous crop in only eight efficacy trials. The previous seasons crop in all other trials was either maize (n = 21) or a late-planted maize trap crop (n = 40) to maximize the probability of CRW egg deposition and larval-feeding pressure for the following season's efficacy trial. Experimental plots were planted with a variety of tillage methods (spring chisel plow, disk, field cultivator, etc) representative of recommended practices, see Supplementary data (online) for additional details. Herbicides were applied as needed and following local agronomic practices.

Selection Criteria

The following a priori criteria were selected for inclusion of a treatment in the meta-analysis. First, a treatment must have been used for a minimum of three growing seasons irrespective of location. Second, a treatment must have been used at a minimum of two locations. Third, only treatments with greater than 10 separate treatment means were included. These considerations were included to limit the effect of extreme growing conditions (drought, flood, high growing temperature, etc.) across space and time and their effects on variability. All insecticides were converted to AI/m to standardize and group granular and liquid insecticides across trade names and delivery methods whereas insecticidal seed treatments were grouped by AI per kernel, as AI/m would vary with plant population (i.e., seeds/m of planted row) (Table 1). Small plot studies would often provide multiple treatment means of a given compound AI/m as multiple delivery methods (liquid vs. granular), delivery locations (parallel to or in line with the seed), insecticide brands ('name" brand versus generic), and/or hybrids may have been tested within a given study. Large plot studies only provided one treatment mean per compound AI/m.

Meta-analytical Model

Analyses of yield, stand count, and root damage were conducted on all studies that fit the previous selection criteria. While yield is the most critical ultimate measure of pesticide effectiveness, it does not

Table 1. Compounds included in meta-analyses

Compound	Rate (mg ai/m)	Treatment abbreviation	IRAC group	GUS risk[1]	Years used	Cost ($/ha) avg±SD	No. values used in cost calculation
Bifenthrin	6.98	BIFEN low	3A	Low	2000–2007	35.32 ± 5.60	9
Bifenthrin	8.56	BIFEN high	3A	Low	2001, 2003–2005	42.78 ± 6.55	9
Chlorethoxyfos	13.95	CHLETH low	1B	Low	2000–2003	N/A	N/A
Chlorethoxyfos	17.21	CHLETH high	1B	Low	2002–2007	N/A	N/A
Chlorpyrifos	111.61	CHLPYR	1B	Low	2000–2007, 2010, 2011, 2013–2015	43.47 ± 10.19	7
Cry3Bb1	N/A	CRY3Bb1	11A	N/A	2003–2004	N/A	N/A
Fipronil	11.16–12.09	FIP	2B	Med	2000–2006	N/A	N/A
Clothianidin	6.52–7.77	1.25 CLO	4A	High	2001–2011, 2013–2015	17 to 52[2]	N/A
Imidacloprid	6.99–8.33	IMID	4A	High	2000–2002	N/A	N/A
Tebupirimphos/ Cyfluthrin	13.02–13.67	TEBU/CY	1B/3A	Med/low	2000–2007, 2010, 2011, 2013–2015	62.87 ± 6.63	15
Tefluthrin	11.161	TEFLU	3A	Low	2000–2007, 2010, 2011, 2013–2015	63.08 ± 8.92	11
Terbufos	111.61	TERB	3A	Low	2000–2004, 2007, 2011	65.55 ± 7.67	7

[1] All GUS values reported from Pesticide Properties Database (2017).

[2] Estimates range from ~$17/ha (Studebaker 2007) to ~$52.36/ha (North et al. 2017).

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allow for assessment of when or how pest damage occurs. This omission can lead to a higher probability of incorrectly attributing a yield increase to a pesticide choice when it is really the result of compensatory growth masking pest damage (Kahler et al. 1985, Lemcoff and Loomis 1994), subeconomic levels of insect feeding or other factors. To increase resolution, stand counts may be performed early in the growing season to indirectly assess the abundance of early season pests and/or phytotoxicity by comparing the number of kernels planted with the percentage of plants found in a subsequent survey. While two different CRW scales [0–3 point (Oleson et al. 2005) and the Iowa 1–6 scale (Hills and Peters 1971)] were used to quantify CRW damage to maize plants, no detailed methods have been developed for secondary pests, perhaps because they are not commonly found at economically damaging levels in most fields (Royer et al. 2004). Consequently, only CRW damage was assessed. Analyses were conducted on both the 0–3 scale in years 2002–2015 and the 1–6 scale from 2000 to 2004; the 0–3 scale was fully implemented as the standard beginning in 2005.

All meta-analyses and effect sizes were calculated with the *metafor* package version 1.9–9 (Viechtbauer 2010) in R 3.4.0 (R Core Team 2017). Effect sizes (Hedges' *g*) were calculated with the *escalc* function using the standardized mean difference estimator. In addition to correcting for small sample sizes, this approach divides the difference between the treatment mean and comparator mean, by the pooled variance to produce an effect size (Hedges 1981). Two different comparators were used, an untreated control (UTC) and a Poncho 250 rate, in which the rate of 0.25 mg/kernel of CLO was applied (0.25 CLO). While 0.25 CLO contains a nominal level of insecticide and is thus not a true 'control,' the inclusion of this comparison set is justified as the 0.25 CLO rate is the lowest rate of treated seed conventional growers have access to; untreated seed is largely absent as an option for U.S. maize producers (Krupke et al. 2012, Douglas and Tooker 2015). Furthermore, as a UTC was unavailable for comparison in some years, inclusion of a 0.25 CLO comparator allowed us to utilize the data from these years. All other years (00–06, 10, 15) used a UTC for effect size calculation, however, whenever 0.25 CLO was used in years alongside an UTC (01, 02, and 15), those data were also used in the 0.25 CLO comparisons. Most of the 2008 data could not be used as most sites/year planted seed treated with a 0.25 CLO rate in addition to any further applied soil insecticides. This management decision made it impossible to separate the joint 0.25 CLO/insecticide effect into its respective constituents. Similarly, 2012 data could not be used as no control (0.25 CLO or UTC) was used that year.

Random Effects Model

The *rma.mv* function in *metafor* was used to calculate the results of each meta-analysis with a restricted maximum likelihood estimator. A random effects model was first used to assess the overall effect of insecticides at CRW rates and used 'site-year' as a random factor. A site-year was defined as all comparisons that took place within the same trial, year, and location. For example, even if a given trial had two different hybrids with respective controls (as in 2003 small plots, where hybrids RX708 and NK N72-V7 were planted together), they would still be considered the same site-year as they shared all site attributes except hybrid, although a hybrid-specific effect size was still calculated. If an agricultural center had both large and small plots planted within the same year, they would be considered separate site-years.

Concern of publication bias, otherwise known as the "file drawer problem" in which nonsignificant studies are not published (Rosenthal 1979), is not a key concern, as none of these analyses were published previously in peer-reviewed journals. Despite this, and to remain conservative in our analysis, the fail-safe number for each significant analysis was calculated according to Rosenthal's method (1979) at an α of 0.05 and represents the number of nonsignificant studies that would need to be included in the meta-analysis to change the results from significance to nonsignificance. Fail-safe numbers are considered robust if $>5n+10$ with n representing the number of studies within the meta-analysis.

Mixed Effects Model

Following the random effects models, each plant health metric was analyzed with a mixed model using "AI/m" as a fixed categorical factor and "site-year" as the random factor. A list of tested compounds and abbreviations can be found in Table 1. Differences between each tested insecticide were assessed with an omnibus test of between-group heterogeneity (Q_b) and compared against a χ^2 distribution with differences considered significant at $P < 0.05$. The mean effect was plotted along with confidence intervals, and treatment significant differences were determined from overlap of confidence intervals with both the comparator line and other mean AI/m effect sizes.

Economic Analysis

To facilitate economic analyses across all site-years, the proportional yield was calculated for each treatment mean within a given site-year. This was done by dividing each treatment's mean yield, by the treatment with the largest treatment mean yield, for the respective hybrid at that given site-year. In this manner, yields represent a proportion of the maximum treatment yield in that site-year. Next, a treatment-associated yield benefit was calculated by taking the difference between a treatment's mean proportional yield and the mean proportional yield of the corresponding control. All yield benefit data for a given compound were then analyzed with a *t*-test to calculate the mean treatment effect (TE) and its standard deviation (TE_{SD}) as in the study by Esker and Conley (2012) and Krupke et al. (2017). Both variables (TE and TE_{SD}) were used to calculate the mean net expected return (μ) and its SD (σ) in $/ha as follows:

$$\mu = MP \ x \ Y \ x \ TE \ - \ IC$$

and

$$\sigma = MP \ x \ Y \ x \ TE_{SD}$$

where Y represents the average Indiana yield from 2010 to 2015 (9.59 mt/ha; USDA-NASS 2017a), MP as the average Indiana sale price from 2010 to 2015 (203.93 $/mt; USDA-NASS 2017b). A 5-yr average for both Y and MP was used to account for annual variability in prices. Insecticide cost was represented by IC and was estimated with telephone surveys conducted in January 2017 with various vendors listed in the Indiana State Chemist's Restricted Use Pesticide dealer database. Vendors were selected based on proximity to each of the five agricultural field stations and must have been adjacent to or within the same county as the agricultural field station. Data from at least two vendors per research station were used. Current (winter 2016) insecticide prices were reported as none of the surveyed vendors were able to provide historical price data.

Both μ and σ were used to parameterize a probability density function of the form:

$$f(x;\mu,\sigma^2) \ = \ (1/\sqrt{2\pi(\sigma * \sigma)})e - 0.5(x - \mu/(\sigma * \sigma))$$

Finally, the cost-relative yield (CRY) was calculated as:

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$$CRY = IC / (MP \ x \ Y)$$

representing the minimum yield increase percentage needed to recover treatment costs and serve as a point within the probability distribution to calculate the one-tail breaking even probability.

The average price of *MP* and *IC* ± 1 SD was used to provide a price range on which economic feasibility could be calculated (Table 1) resulting in the CRY being calculated under nine different economic conditions (three different *MP* × three different *IP*) for each insecticide. The 1.25 CLO rate could not be estimated as NSTs are applied before sale to the grower and the cost of this service is not disclosed in the marketing of maize seed in North America. Estimated costs range from $52.36 (North et al. 2017), ~$39.5–47/ha (Shields 2003), $37.5/ha (Seagraves and Lundgren 2012), ~$34.6–42/ha (Bessin 2003), and ~$17/ha (Studebaker 2007) so the break-even probability was calculated under prices similar to this range.

Results

Random Effects Model

Use of a CRW rate insecticide, regardless of AI, led to significant decreases in node damage and significant increases in stand and yield as evidenced by the overall effect on each plant health metric with a UTC comparator (Table 2). Of the two metrics assessed with a 0.25 CLO comparator, only node damage was significantly reduced, with no significant change in stand count from the 0.25 CLO comparator (Table 2). The mean effect of all tested CRW insecticides resulted in significant decreases in root damage (Oleson: Hedge's $g = -1.86$ $P = <0.0001$; Iowa: Hedge's $g = -1.84$ $P = <0.0001$) and significant increases in yield (Hedge's $g = -0.82$ $P =<0.0001$) when a UTC was used. Only root damage was significantly reduced with a 0.25 CLO comparator (Hedge's $g = -0.97$ $P = 0.001$). All significant models had robust fail-safe numbers >5,000, indicating a large number of nonsignificant studies would need to be included to change significant results to nonsignificance (Table 2).

Mixed Effects Model

Significant heterogeneity was observed between effect size means in models analyzing root damage (Oleson: $Q_b = 18.333$ $P = 0.049$; Iowa: $Q_b = 44.317$ $P < 0.0001$), stand ($Q_b = 48.265$ $P < 0.0001$) but not in yield ($Q_b = 5.502$ $P = 0.703$) with the use of a UTC comparator. In the stand model, the 1.25 CLO effect size mean significantly increased stand counts in comparison to most other effect size means (Fig. 1b) as determined by CI overlap. As the effect size CI of each AI/m overlaps in the Oleson model, it is impossible to determine where between group differences lie (Fig. 2a). In contrast, both the TEBY/CY and Cry3Bb1 treatments significantly reduced root damage on the Iowa scale in comparison to the Fipronil mean effect size (Fig. 2b). When a P250 comparator was used to describe stand changes and root damage, significant heterogeneity was only observed in the stand model (Stand: $Q_b = 14.789$ $P = 0.011$; Oleson: $Q_b = 5.690$ $P = 0.224$). It is likely the 1.25 CLO treatment significantly increases stand counts in comparison to at least one other AI/m effect size mean, but again, as the CI of each AI/m effect size overlaps, it is impossible to determine which comparisons are significant.

When compared to the UTC effect line (Hedge's $g = 0$), all tested CRW insecticides significantly increased yield (Fig. 1a) and decreased node damage on both the Oleson (Fig. 2a) and Iowa (Fig. 2b) scale as evidenced by the lack of overlap of CI with UTC effect line. In the UTC stand model (Fig. 1b), all insecticides with the exception of imidacloprid (IMI) and 1.25 CLO did not significantly increase stand in comparison to a UTC. When insecticides were tested with a P250 comparator, all tested insecticides significantly decreased root damage (Fig. 3a) but did not significantly alter stand counts (Fig. 3b).

Economic Analysis

Six compounds could be assessed with the economic analysis (Table 3). Both Fipronil and the Chlorethoxyfos treatments (Table 1) were not included despite their inclusion in the meta-analysis (Fig. 1a) as these compounds have been off market for several years and no price estimates were available. A high probability (>80%) of breaking even was associated with all tested compounds under varying market conditions (Table 3). The CRY for all treatments was <5% in the vast majority of cases indicating an insecticide would only have to increase the yield by a marginal amount to recover the seed and insecticide costs (Table 4). Likewise, the expected economic return for each treatment associated mean is presented in Table 5.

Discussion

This analysis reveals that while the NST treatment was the only set of compounds to result in higher stand counts (Fig. 1b), this advantage was not borne out by other comparison parameters, including yield. The NSTs 1.25 CLO and IMI were the only compounds tested that led to significantly higher stand counts with an UTC comparator (Fig. 1b), but not with a 0.25 CLO comparator (Fig. 3b), although the presence of fungicide seed treatments in these treatment is an important confounding factor. All other compounds failed to increase stand in comparison to their respective comparator (UTC: Fig. 1b; 0.25 CLO: Fig. 3b). Given the overlap between 1.25 CLO CI with a 0.25 CLO comparator line (Fig. 3b), it is also a possibility that the stand protection NSTs provide is not rate dependent, at least

Table 2. Mean effect size of insecticide related changes in various crop health metrics using two different comparators (UTC and 0.25 CLO)

Comparator[1]	Metric	Avg Hedges' *g*	CI	*Z*	*P*-value	No. of site-years	Fail-safe No.[2]
UTC	Stand	0.16	0.15	2.15	0.03	55	8778
UTC	Node 3	−1.86	0.43	−8.58	<0.0001	40	420035
UTC	Node 6	−1.84	0.33	−11.00	<0.0001	35	419124
UTC	Yield	0.82	0.23	6.97	<0.0001	31	22137
0.25 CLO	Stand	−0.004	0.34	0.02	0.98	21	0
0.25 CLO	Node 3	−0.97	0.58	−3.30	0.001	18	5211

All models assessed the effect of insecticides at CRW rates and used the no. of site-years as a random factor.

[1] Two different comparators were used: Untreated control (UTC) and a 0.25 mg of clothianidin per kernel rate (0.25 CLO).

[2] Calculated using the Rosenthal method (1979).

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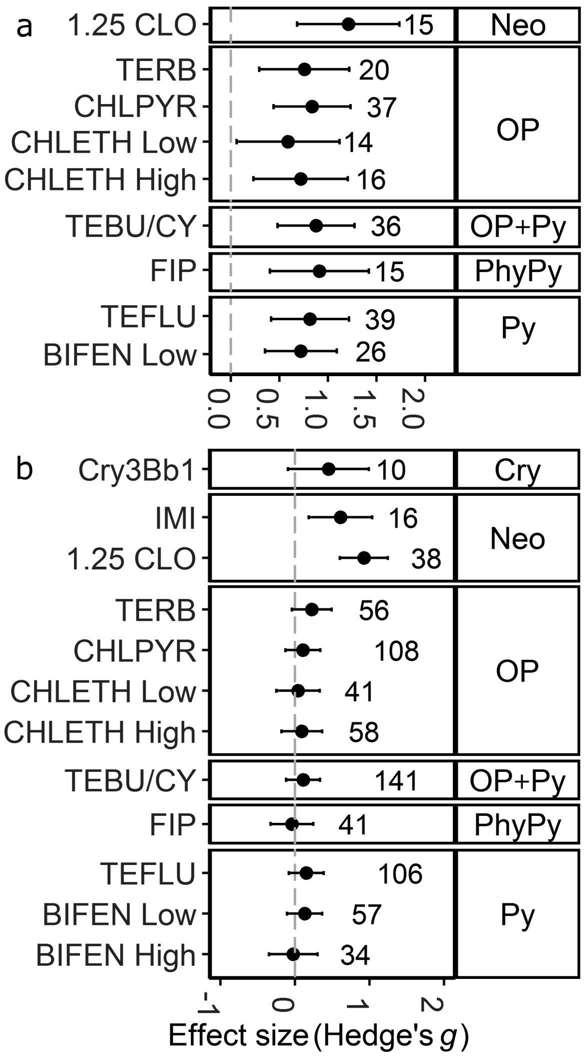

Fig. 1. Effect of insecticide on yield (a) and early-season stand counts (b) in comparison to an untreated comparator. The number of replicates used to calculate effect size are adjacent to each bar. 95% confidence intervals are shown.

between these two rates. There were too few studies that included a 0.25 CLO rate in the UTC meta-analyses so we cannot determine if the 0.25 CLO rate significantly increases stand counts in comparison with the 1.25 CLO rate. Interestingly, while this finding reaffirms young plant protection can be provided by NSTs (Elbert et al. 2008), the 1.25 CLO stand increase did not lead to higher yields than compounds that did not increase stand (Fig. 1a). This observation is possibly the result of compensatory growth in treatments with lower stand counts, which has been well documented in maize (Kahler et al. 1985, Lemcoff and Loomis 1994) or subeconomic levels of feeding. Finally, it is important to note that the stand increase may be at least partially attributable to the suite of fungicides applied to seeds with NSTs. All other insecticide treatments did not receive a fungicide treatment in the vast majority of site-years used in this study, whereas the NSTs likely did. We cannot definitively conclude that a seed applied fungicide was included with the NSTs used in the project as the bag tags, which detail the AIs within the seed treatment, had been discarded years before this project began. Despite this, NSTs are rarely sold without included seed-treated fungicides and, therefore, we believe this is a relatively safe assumption. This is a key limitation of the study and means that it is not possible to separate out the relative contributions of NST and fungicide to stand increases we report here; future studies focused on untangling the relative contributions of NST and seed-applied fungicides would be useful.

Another finding worth noting is the overall similarity of results between the Oleson and Iowa scales with a UTC (Fig. 2). While significant differences were recorded in the Oleson model, the overlap of CI between tested compounds made determining treatment differences impossible. This was not the case for the Iowa scale where the Cry3Bb1 and TEBU/CY treatments decreased damage more than the BIFEN high treatment (Fig. 2b). This minor difference may be due in part to a difference in data sets analyzed (Iowa: 2000–2004; Oleson: 2002–2007, 2010, and 2015). However, this explanation is unlikely as high CRW pressure (defined as an UTC root rating >0.5 and >3 on Oleson and Iowa scales, respectively) was reported in a similar proportion of site-years in both analyses (Iowa: 62.9%; Oleson: 76.7%). Additionally, 20 of the 35 and 43 site-years were shared between the Iowa and Oleson scale analyses, respectively, limiting

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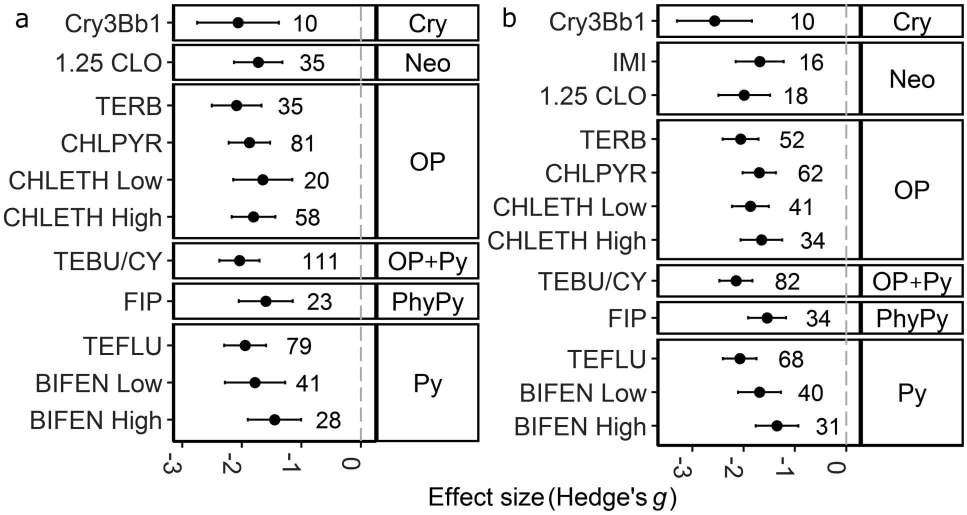

Fig. 2. Effect of insecticide on node damage as measured on the Oleson 3-point scale (a) and Iowa 6-point scale (b) in comparison to an untreated comparator. The number of replicates used to calculate effect size are adjacent to each bar. 95% confidence intervals are shown.

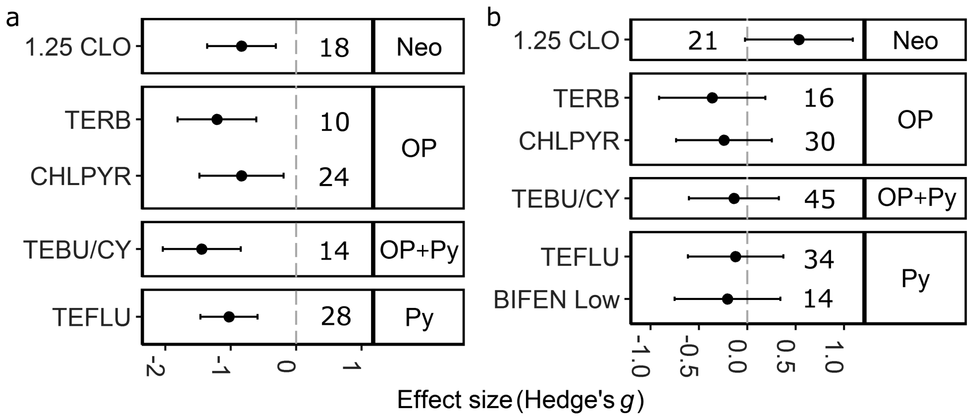

Fig. 3. Effect of insecticide on node damage as measured on the Oleson 3-point scale (a) and early season stand counts (b) in comparison to a 0.25 CLO comparator. The number of replicates used to calculate effect size are adjacent to each bar. 95% confidence intervals are shown.

Table 3. Breaking even probability of different prophylactic insecticides under varied maize sale prices (2010–2015 Indiana sale price X̄ ± 1 SD) and insecticide costs (Vendor X̄ ± 1 SD)

Maize sell		Insecticide cost ($/ha)				Insecticide cost ($/ha)		
Price ($/mt)	Compound	29.72	35.31	40.92	Compound	33.28	43.47	53.66
149.21	BIFEN low	0.993	0.989	0.982	CHLPYR	0.997	0.992	0.981
203.93	BIFEN low	0.996	0.995	0.993	CHLPYR	0.999	0.998	0.995
258.26	BIFEN low	0.998	0.997	0.996	CHLPYR	0.999	0.999	0.998
	Compound	56.23	62.86	69.50	Compound[1]	20.00	40.00	60.00
149.21	TEBU/CY	0.954	0.926	0.885	1.25 CLO	0.995	0.983	0.946
203.93	TEBU/CY	0.988	0.981	0.980	1.25 CLO	0.997	0.991	0.978
258.26	TEBU/CY	0.995	0.992	0.989	1.25 CLO	0.998	0.994	0.988
	Compound	57.88	65.55	73.22	Compound	54.16	63.08	72.00
149.21	TERB	0.912	0.871	0.818	TEFLU	0.989	0.974	0.944
203.93	TERB	0.965	0.950	0.931	TEFLU	0.999	0.995	0.990
258.26	TERB	0.981	0.974	0.965	TEFLU	0.999	0.999	0.997

[1] Estimates range from ~$17/ha (Studebaker 2007) to ~$52.36/ha (North et al. 2017) so a range of prices was tested.

the impact of nonshared years. A more likely scenario is how both scales grade damage. The Iowa scale is qualitative and nonlinear whereas the Oleson scale is quantitative and linear (Oleson et al. 2005). Therefore, a root with an injury score of three exhibits double the injury of a root with a score of 1.5 on the Oleson scale, unlike the Iowa scale. In addition to its nonlinearity, the Iowa scale poorly describes injury equivalent to <1 node. As a result, the effect size of a given treatment is artificially inflated when the comparator has >1 node worth of damage and a treatment has <1 node of damage. A more complete description of how the Oleson and Iowa scale differ in how injury is scored can be found in Oleson et al. (2005).

Of course, it is possible that pest pressure differences between these year ranges can account for part of this result. One hypothesis is that pests were more common before widespread NST and Bt use and the comparatively lower pressure in later sampling years is the result of area-wide suppression, as shown in the European corn borer response to widespread Bt adoption (Hutchison et al. 2010). For example, Bt maize hybrids targeting CRW were first introduced during the growing season of 2004, and their rapid and widespread adoption may have led to regional declines in CRW pressure. Similarly, it has been suggested that widespread NST adoption in soybeans has led to area-wide suppression of soybean aphid (Bahlai et al. 2015). Although no data exist to support or refute this hypothesis in CRW or other, secondary pests of maize, it is plausible, given the rapid and nearly complete adoption of NST in maize, soybeans, and other annual crops over the last 10–15 yr.

Our economic results differ slightly from a recent analysis on the economic benefits of NST in the mid-south from 2001 to 2014 which found NST increased yield by an average of 700 kg/ha, corresponding to an 8.2% increase in yield and an economic return of $56/ha when compared to a fungicide-only treatment (North et al. 2017). In contrast, our NST-associated yield increase was 8.7%, with a corresponding economic return of $64.4–195.7/ha under each of our *IC* and *MP* combinations (Table 5) when compared to a UTC. Assuming a NST cost of $52.36/ha for the CRW rate (North et al. 2017), our economic return changes to $72, $117.7, and $163.3/ha for our respective price points of $149.21, $203.93, and $258.26/mt (calculations not shown in table). Part of why our economic return differs from North et al. (2017), despite a similar increase in yield, is how both studies calculated the yield sale price. In the study by North et al. (2017), the yield of each treatment (NST, fungicide) was multiplied by the average sale price of the corresponding year and state for each efficacy trial, with the cost of the NST being subtracted from the gross economic return. As maize prices fluctuated widely over the 2001–2014 period in the mid south (min: $80/mt max: $290/mt), years in which large economic returns were reported are partially suppressed by years in which smaller economic returns were reported. In contrast, our study took the average maize sale price Indiana growers received from 2010 to 2015 which included historically high maize sale prices. This artificially increased our mean *MP* ($203.93/mt) but we accounted for this by testing a range of *MP*.

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Table 4. The cost relative yield of different prophylactic insecticides under varied maize sale prices (2010–15 Indiana sale price X̄ ± 1 SD) and insecticide costs (Vendor X ± 1 SD)

Maize sell		Insecticide cost ($/ha)				Insecticide cost ($/ha)		
Price ($/mt)	Compound	29.72	35.31	40.92	Compound	33.28	43.47	53.66
149.21	BIFEN low	2.08	2.47	2.86	CHLPYR	2.33	3.04	3.75
203.93	BIFEN low	1.52	1.81	2.09	CHLPYR	1.70	2.22	2.75
258.26	BIFEN low	1.20	1.42	1.65	CHLPYR	1.34	1.75	2.16
	Compound	56.23	62.86	69.50	Compound[1]	20.00	40.00	60.00
149.21	TEBU/CY	3.93	4.40	4.86	1.25 CLO	1.40	2.80	4.20
203.93	TEBU/CY	2.88	3.22	3.56	1.25 CLO	1.02	2.05	3.07
258.26	TEBU/CY	2.27	2.54	2.80	1.25 CLO	0.81	1.61	2.42
	Compound	57.88	65.55	73.22	Compound	54.16	63.08	72.00
149.21	TERB	4.05	4.58	5.12	TEFLU	3.79	4.41	5.04
203.93	TERB	2.96	3.35	3.75	TEFLU	2.77	3.23	3.68
258.26	TERB	2.33	2.64	2.95	TEFLU	2.18	2.54	2.90

This represents the minimum yield increase percentage needed to recover treatment costs.

[1] Estimates range from ~$17/ha (Studebaker 2007) to ~$52.36/ha (North et al. 2017) so a range of prices was tested.

Table 5. The mean expected economic return per hectare ($/ha) as a consequence of using a prophylactic insecticide in comparison to an UTC

Maize Sell		Insecticide cost ($/ha)				Insecticide cost ($/ha)		
Price ($/mt)	Compound	29.72	35.31	40.92	Compound	33.28	43.47	53.66
149.21	BIFEN low	80.3	74.7	69.1	CHLPYR	79.6	69.5	59.3
203.93	BIFEN low	120.7	115.1	109.5	CHLPYR	121.1	110.9	100.7
258.26	BIFEN low	161.1	155.5	149.9	CHLPYR	162.5	152.3	142.1
	Compound	56.23	62.86	69.50	Compound[1]	20.00	40.00	60.00
149.21	TEBU/CY	45.8	39.2	32.6	1.25 CLO	104.4	84.4	64.4
203.93	TEBU/CY	83.4	76.7	70.0	1.25 CLO	150.0	130.0	110.0
258.26	TEBU/CY	120.7	114.1	107.5	1.25 CLO	195.7	175.6	155.6
	Compound	57.88	65.55	73.22	Compound	54.16	63.08	72.00
149.21	TERB	46.5	38.8	31.2	TEFLU	58.8	49.9	40.9
203.93	TERB	89.8	77.1	44.8	TEFLU	100.2	91.3	82.4
258.26	TERB	123.1	115.4	107.7	TEFLU	141.6	132.7	123.8

Calculations used varied maize sale prices (2010–2015 Indiana sale price X̄ ± 1 SD) and insecticide costs (Vendor X̄ ± 1 SD).

[1] Estimates range from ~$17/ha (Studebaker 2007) to ~$52.36/ha (North et al. 2017) so a range of prices was tested.

Our tests were conducted using commercially available products and rates representative of what growers in the state of Indiana may use to manage key pests. Across all studies, the 1.25 CLO AI/m ranged from 6.52 to 7.77 mg/m corresponding to a planting rate of 38,910–46,354 KPH meaning only the low BIFEN treatment possessed a lower AI/m (Table 1). While this finding suggests that ST use decreases the high dose rates associated with in-furrow application or sprays (Elbert et al. 2008), the rapid and thorough adoption of NSTs has actually increased the percentage of maize hectares treated with insecticide (>75% in 2011) (Douglas and Tooker 2015).

Our data reflect the similarity of insecticide performance across multiple metrics and the high probability of breaking even economically. This suggests that, instead of the current annual use pattern that govern NST use in maize, they could be readily incorporated into a grower's insecticide rotation when managing the key pest of maize in Indiana and across much of North America. Alford and Krupke (2017) recently estimated the protection window NSTs provide to the seed and root region of young maize; it is possible that NST concentrations in plant tissues may have intersected with damaging pest populations to generate the stand increases summarized in Fig. 1b. Although no estimates of secondary pest infestations were made during our data collection, wireworm and seedcorn maggot activity periods are well correlated with the high in-plant concentrations of CLO in the seed region (Alford and Krupke 2017). While NSTs can be used for seed protection, their mandatory use is frequently superfluous as wireworms remain an occasional pest across most of the country (Royer et al. 2004) and the likelihood of occasional seedcorn maggot infestations can be predicted based on incorporation of a green cover crop into the soil (Hammond 1990). A grower should be able to decide if an NST is required based on their individual risk from these seed pests. Finally, while NSTs can provide some control of early-season root pests, high concentrations of in-plant CLO are not well correlated with CRW phenology (Alford and Krupke 2017). The similarity in root protection (Fig 2a and 2b), coupled with the high probability of breaking even economically (Table 3), indicates that NSTs can easily be incorporated into a grower's insecticide rotation when managing for CRW.

While our study suggests that NSTs can be readily incorporated into a grower's insecticide rotation when managing CRW damage within Indiana, Tinsley et al. (2015) suggested rotation of single-trait Bt and soil insecticides as a viable CRW management strategy. NSTs were not included in their rotation recommendation as they did not perform as well as in our study. An explanation was not provided for the poor performance of NSTs in the study by Tinsley et al. (2015) but is likely at least partially attributable to historically greater CRW

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pressure experienced by the states (Illinois and Nebraska) used in their analyses. An estimate of cropping patterns can be derived from satellite data accessible on the USDA-NASS CropScape website (Han et al. 2012). A greater portion of both Illinois and Nebraska farmland favor continuous maize cropping whereas Indiana has a greater adoption of maize/soy rotation. As such, it is a possibility that our rotation recommendations can only be applied to areas in which crop production is routinely practiced and CRW pressure is relatively low; this includes much of the corn production area from Indiana eastward.

While NST are not a primary approach for CRW control, their continual use may eventually render them completely ineffective. The continual maize cropping patterns of the western corn belt led to a reliance on chemical means of CRW control (Pereira et al. 2015) with subsequent resistance to aldrin (Ball and Weekman 1962), methyl parathion (Meinke et al. 1998), carbaryl (Meinke et al. 1998), and bifenthrin (Pereira et al. 2015) by the target pest. A similar fate may be in store for the neonicotinoids, which are not only effectively mandated by maize seed distributors, but an increasing proportion of soybean seed sold in the United States is being treated with NSTs as well (Douglas and Tooker 2015). This means that even in areas in which maize is rotated with soy, the field soils where CRW larvae spend their entire life cycle experience a repeated and continual dose of neonicotinoid insecticides. The adaptability of CRW in responding to selection pressures has been demonstrated repeatedly by the rapid evolution of resistance to not only insecticides but also to cultural practices such as crop rotation [both delayed diapause (Krysan et al. 1986) and soybean variant oviposition (Levine and Oloumi-Sadeghi 1996)]. Growers are not provided ready access to untreated seed across the United States (Douglas and Tooker 2015) despite what is known about CRW resistance potential. Ideally, insecticides would be treated as a limited, finite resource (Sparks and Nauen 2015) and aim to slow the development of resistance by judicious use. We provide data here that suggest that, in the case of NST use relative to CRW, rotation is achievable without exposure to yield losses. Finally, it is worth noting that we are unaware of any areawide resistance monitoring programs for NST with respect to CRW.

This study demonstrates that, while NSTs are ubiquitous on corn, their contribution to yield and root protection from CRW is no better than established chemistries in Indiana across multiple sites and years. However, unlike the other chemistries in our study, NST use is not an elective choice for U.S. corn producers and is rarely the only approach deployed against insect pests. Our data analyses do not justify the widespread application and use of NSTs in maize partly because they are almost always deployed along with other approaches, such as Bt hybrids [with Bt hybrids accounting for 77% of U.S. maize by area planted in 2017 (USDA-NASS 2017c)] and/or some of the insecticide classes included in our study. A potential, largely unexamined negative aspect of this approach is that the repeated prophylactic use of a single insecticide chemistry is likely to accelerate resistance, partially nullifying benefits associated with NST use. While attempts to maintain the utility of Bt maize and soil insecticides have been made by planting refuges and rotating AIs, respectively, neither option is readily available to growers in mitigating the resistance potential of NSTs as they are unable to purchase untreated seed. This lack of choice is difficult to justify, given the apparent redundancy of NST with other available control tactics, coupled with the potential for negative outcomes that typically follow widespread and continuous use of any class of insecticides.

Supplementary Data

Supplementary data are available at *Journal of Economic Entomology* online.

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