Data Driven Enhancements to the Intestinal Integrity ($I^2$) Index: A Novel Approach to Support Poultry Sustainability

Alexandra L. Swirski $^{1,2}$, Hind Kasab-Bachi $^2$, Jocelyn Rivers $^{1,2,*}$ and Jeffrey B. Wilson $^2,*$

1 Department of Population Medicine, Ontario Veterinary College, University of Guelph, Guelph, ON N1G 2W1, Canada; aswirski@uoguelph.ca (A.L.S.); jrivers@uoguelph.ca (J.R.)
2 Novometrix Research Inc., 4564 Nassagaweya-Puslinch Townline, Moffat, ON L0P 1J0, Canada; hind.bachi@novometrix.com
* Correspondence: jbwilson@novometrix.com; Tel.: +1-519-824-7771

Received: 16 June 2020; Accepted: 11 July 2020; Published: 1 August 2020

Abstract: Background: Optimizing the intestinal integrity of poultry flocks through a comprehensive index measure, such as the intestinal integrity ($I^2$) index, could help to promote sustainable production in the poultry industry. The $I^2$ index is a tool for assessing the intestinal health of flocks based on flock level health and performance data, captured by Elanco Animal Health’s global surveillance system, i.e., the Health Tracking System (HTSi). The objectives of this study were to evaluate the relationships between the proposed $I^2$ index and each of the following four performance parameters: average daily gain (ADG), feed conversion ratio (FCR), European production efficiency factor (EPEF), and percent livability; and compare the ability of the proposed $I^2$ index to predict these performance parameters with the current $I^2$ index. Results: The proposed $I^2$ index was found to produce a greater range and increased variation in flock level $I^2$ index scores as compared with the current $I^2$ index. The proposed $I^2$ index was found to predict the four performance measures at least as well as the current $I^2$ index. Conclusions: Our results highlight the strength of data-driven approaches in the development and improvement of comprehensive health metrics.

Keywords: poultry; intestinal integrity; performance; intestinal index

1. Introduction

Contemporary agriculture, including the global poultry industry, faces enormous challenges due to a growing demand for animal protein compounded by pressures from consumers for the industry to become more sustainable and transparent [1–3]. Due to an increasing demand for meat products as a result of increased consumer wealth and population growth, the global chicken population has grown by approximately 4.5-fold over the past 50 years [2,4]. Production demands are expected to rise even more drastically in the near future as the world population is projected to reach nine billion by 2050, and animal production is expected to grow to fulfill the global demand [2,5,6]. As a result of the growing concern surrounding food security, there has been a shift towards long-term sustainability of poultry production, based on being economically profitable, ecologically sound, and socially acceptable [6,7]. These three pillars of sustainability are captured by the One Health paradigm, which aims to focus on interrelatedness among animal, human, and environmental health [8]. It has been previously suggested by Briault [9] and Perez [6] that the next challenge under the One Health paradigm would be the use of applied quantitative epidemiology and economics, and that the fundamental economic assumptions of One Health needed to be re-examined in order to allow for effective international
improvements in human, animal, and ecosystem health. Thus, the role of economics in One Health and sustainability of the global poultry industry cannot be overstated. However, identifying and adopting sustainable solutions rely on a wide variety of stakeholders and are complicated by the interconnectedness of production systems and trade at a global level [6]. Adoption of an integrated health economics approach (i.e., linking diseases to economics and subsequently offering solutions to increase profitability), could be the most effective starting point for an integrated One Health approach to sustainability in the poultry industry.

Commercially sustainable poultry production relies on maintaining flock health through effective pathogen control, including effective biosecurity, animal husbandry, management practices, prophylaxis, and vaccination [10,11]. Optimal intestinal integrity is especially important, as a healthy intestinal system promotes sustainability through reduction of resources required for production via optimized feed usage and reduction of nutrient waste [10]. Intestinal diseases such as necrotic enteritis, gizzard erosion, and coccidiosis can have significant negative effects on productivity via impaired feed conversion ratios (FCR), and increased morbidity and mortality [11–15]. Consequently, intestinal diseases represent a significant economic burden to the global poultry industry and result in an estimated USD 2 billion in economic losses annually, worldwide [16–18]. It has been suggested that optimized intestinal health, and as a result production optimization, would promote all three pillars of sustainability through decreased resource utilization and increased consumer access to safe and affordable food [19].

Optimizing the intestinal integrity of poultry flocks through the use of a platform-based comprehensive index measure, such as the intestinal integrity ($I^2$) index developed by Elanco Animal Health (Greenfield, Indianapolis, IN, USA) could help to support sustainable production in this industry. The $I^2$ index is currently used to inform producers of potential interventions required to improve the intestinal health of their flocks, thereby increasing flock performance, welfare, and profitability (i.e., sustainability). The $I^2$ index is a constantly evolving, comprehensive, and producer-friendly means of assessing the intestinal health of flocks. The index consists of the following 23 intestinal conditions known to impact intestinal health: necrotic enteritis, gross *Eimeria acervulina*, gross and microscopic *Eimeria maxima*, gross *Eimeria tenella*, gross *Eimeria brunetti*, gross *Eimeria mitis*, gross *Eimeria necatrix*, gizzard erosion, proventriculitis, mouth lesions, roundworms, tapeworms, intestinal tone, intestinal fluid, thin intestine, thick intestine, excessive bile, excessive intestinal mucus, cellular sloughing, feed passage, hyperemia, and intestinal hemorrhage (Table 1). These health metrics are gathered via a necropsy assessment of five to 20 healthy birds between the ages of six to 56 days, per flock. Samples are collected based on a convenience sample while moving in a zigzag pattern across the barn and visibly sick birds are excluded from sampling. A full descriptive of these methods is provided Kasab-Bachi et al. [19] and clinical diagnoses of all intestinal conditions are based on information available in the standard reference guide developed by Elanco [20]. Results from the necropsy assessments are subsequently used to calculate flock averaged lesion scores for each intestinal condition. The $I^2$ index is, then, calculated by applying a previously proprietary weighting scheme, based on the perceived relative importance of each condition, to the flock averaged lesion scores for each condition within the $I^2$ index [19].

According to the current equation, an $I^2$ index of 100 indicates an absence of all of the above-mentioned conditions, and therefore the closer a flock’s $I^2$ index is to 100, the healthier the flock is. However, it is possible for a flock to be assigned a negative $I^2$ index, if all of the diseases are present.

Previous work by Kasab-Bachi et al. [19] identified statistically significant relationships between the current $I^2$ index and each of the following three key commercial poultry production parameters: average daily gain (ADG), feed conversion ratio (FCR), and the European production efficiency factor (EPEF). However, the researchers found that the current $I^2$ index was not able to adequately predict flock mortality measures, such as percent livability [19]. Although these results suggested that the current $I^2$ index was a valuable tool for predicting key parameters of bird performance,
the researchers recommended a number of potential improvements to further enhance the $I^2$ index. These improvements included: (1) revised lesion scoring systems for conditions that were currently captured as present or absent in order to better capture the spectrum of disease severity, and (2) reassignment of condition weights based on a data-driven approach, instead of the current empirical weighting scheme which was based on a subjective method (i.e., expert opinion) [19]. This $I^2$ index re-evaluation study is funded by Elanco as a One Health project to drive economic sustainability of poultry production and continuously improve tools to add further value for customers.

Table 1. A comparison of the current versus the proposed intestinal integrity ($I^2$) index equations.

| Condition              | Lesion Scoring Scale: Current | Lesion Scoring Scale: Proposed | Conditions by Product of $I^2IS$ and $I^2SS$ |
|------------------------|-----------------------------|-------------------------------|---------------------------------------------|
| Necrotic enteritis     | 0–1                         | 0–2 *                         | 1                                          |
| *Eimeria acervulina*   | 0–4                         | 0–4                           | 3                                           |
| *Macroscopic: Eimeria maxima* | 0–4                       | 0–4                           | 2                                           |
| *Microscopic: Eimeria maxima* | 0–4                       | 0–2 *                         | 2                                           |
| Eimeria maxima         | 0–4                         | 0–4                           | 2                                           |
| Eimeria tenella        | 0–4                         | 0–4                           | 4                                           |
| Eimeria brunetti       | 0–1                         | 0–4 *                         | 5                                           |
| Eimeria mitis          | 0–1                         | 0–1                           | 6                                           |
| Eimeria necatrix       | 0–1                         | 0–4 *                         | 4                                           |
| Gizzard erosion        | 0–3                         | 0–3                           | 2                                           |
| Proventriculitis       | 0–1                         | 0–2 *                         | 6                                           |
| Mouth lesions          | 0–1                         | 0–1                           | 7                                           |
| Roundworms             | 0–1                         | 0–1                           | 6                                           |
| Tapeworms              | 0–1                         | 0–1                           | 7                                           |
| Intestinal tone        | 0–1                         | 0–1                           | 7                                           |
| Intestinal fluid       | 0–1                         | 0–1                           | 4                                           |
| Thin intestine         | 0–1                         | 0–1                           | 6                                           |
| Thick intestine        | 0–1                         | 0–1                           | 7                                           |
| Excessive bile         | 0–1                         | 0–1                           | 7                                           |
| Intestinal mucus       | 0–1                         | 0–1                           | 6                                           |
| Cellular sloughing     | 0–1                         | 0–1                           | 7                                           |
| Feed passage           | 0–1                         | 0–1                           | 6                                           |
| Hyperemia              | 0–1                         | 0–1                           | 7                                           |
| Intestinal hemorrhage  | 0–1                         | 0–1                           | 7                                           |

* Indicates a change to the lesion scoring scale for the proposed, $I^2$ compared to the current $I^2$; 1 Indicates highest product of $I^2IS$ and $I^2SS$.

The $I^2$ index is an emerging, iterative, and practical surveillance tool that is constantly being improved. Therefore, the objectives of this study were as follows: To evaluate the relationships between the proposed $I^2$ index and each of the four flock level performance parameters, i.e., ADG, FCR, EPEF, and percent livability; and compare the ability of the proposed $I^2$ index to predict ADG, FCR, EPEF, and percent livability as compared with the current $I^2$ index.

2. Materials and Methods

2.1. Data Sources

The data for this study were obtained from Elanco Animal Health’s HTSi database (Elanco Animal Health, Greenfield, Indianapolis, USA). Information from the HTSi database was used to construct two separate datasets for subsequent analyses, one at the flock level and one at the individual-bird level.

Flocks for which both health and performance data were available within the HTSi database were collected in the flock-level dataset, as previously described in Kasab-Bachi et al., [19]. All information captured in this dataset was collected at the flock level; the disease-related variables used for the calculation of the $I^2$ index were captured as flock-averaged scores for each condition based on a sample
of five to 20 birds for each flock. Performance parameters (ADG, FCR, EPEF, and percent livability) were also captured at the flock level. This dataset contained information on 3590 healthy flocks from 1500 farms representing 6 USA and 4 UK production flows from 2006 to 2015, inclusive. This dataset was used for all subsequent analyses.

2.2. Proposed Changes to the $I^2$ Index Lesion Scoring Systems

On the basis of a comprehensive review of the literature (unpublished results) and consultation with stakeholders from Elanco, academia, and industry, changes to the lesion scoring system for five of the 23 intestinal conditions within the $I^2$ index (necrotic enteritis, gross *E. brunetti*, gross *E. necatrix*, proventriculitis, and microscopic *E. maxima*) were proposed in order to more effectively capture the spectrum of disease severity and take into consideration the ability to distinguish between severity scores (e.g., a score of two versus a score of three) in the field.

The lesion scoring systems for the remaining 18 intestinal conditions were unchanged; conditions are listed in Table 1. The Broiler Disease Reference Guide is available upon request (20). In addition, the new lesion scores are also available as Supplementary Material and can be obtained on request.

2.3. Proposed Changes to the $I^2$ Index Condition Weights

The weighting scheme of the proposed $I^2$ index is comprised of the following three components based on a data-driven systematic approach: an intestinal integrity importance scale ($I^2$IS), an intestinal integrity statistical scale ($I^2$SS), and a normalization score for each maximum lesion score. The objective of these proposed changes was to increase the weighting of conditions that were highly pathogenic, had high economic importance to the broiler industry, and were statistically associated with key poultry performance measurements.

A comprehensive review of the literature (unpublished results) was used to generate the $I^2$IS. The $I^2$IS reflects the prevalence, pathogenicity, and economic importance of each intestinal condition to the broiler industry by assigning a score of 1–4 for each condition within the proposed $I^2$ index. An $I^2$IS score of 4 was assigned to critically important conditions ($n = 5$), which were defined as priority conditions caused by and organism(s) with a high pathogenicity and could be a major cause of economic concern to the broiler industry. An $I^2$IS score of 3 was assigned to very highly important conditions ($n = 2$), which were defined as priority conditions caused by an organism(s) with moderate pathogenicity and could be a moderate cause of economic concern to the broiler industry. An $I^2$IS score of 2 was assigned to highly important conditions ($n = 3$), which were defined as priority conditions caused by an organism(s) with low pathogenicity and other conditions that were a relatively minor cause of economic concern to the broiler industry. Finally, an $I^2$IS score of 1 was assigned to other important conditions or morphologic diagnosis ($n = 13$) that, on their own, represented a relatively minor economic concern to the broiler chicken industry.

The $I^2$SS was based on the work by Kasab-Bachi et al. [19] which identified statistically significant relationships between the intestinal conditions in the $I^2$ index and each of the following four poultry production parameters: FCR, ADG, EPEF, and percent livability. The proposed $I^2$SS used a 1–4-point scale to weight intestinal conditions based on meaningful associations found between these conditions and each of the five performance outcomes. Therefore, the $I^2$SS score assigned to each condition was based on the number of production parameters it was statistically associated with plus one (in order to avoid a zero weight for a condition), based on the results of the multivariable regression models in Kasab-Bachi et al. [19].

Lesion scores were scaled by normalizing the maximum lesion score for each condition, to ensure morphologic diagnoses and conditions of minor concern did not contribute to an excessive amount of weight within the proposed $I^2$ index formula. Therefore, priority conditions were assigned a normalization score of 4 and other conditions and morphologic diagnoses were assigned a normalization score of 1. The conditions were still evaluated in the field using their unique lesion scoring system which could vary from 0–1 to 0–4; however, the normalization equation was applied within the HTSi
database, prior to calculation of the proposed $I^2$ index. The normalization scores are available as Supplementary Material and can be obtained on request from Elanco Animal Health.

2.4. Proposed $I^2$ Index Equation

According to the proposed revisions to the $I^2$ index, described above, the equation for the proposed Elanco $I^2$ index is an algebraic combination of normalized lesion scores for each lesion in the $I^2$ index, weighted appropriately by the corresponding $I2IS$ and $I2SS$ for each lesion. The final score is then adjusted to ensure that the maximum $I^2$ index is 100, to allow direct comparisons with $I^2$ indices using the original $I^2$ formula. An $I^2$ index of 100 indicates an absence of all of the above-mentioned conditions, and therefore, the closer a flock’s $I^2$ index is to 100, the healthier it is in general; however, it is possible to have a negative $I^2$ index if all diseases are present.

Flock level $I^2$ indexes were subsequently calculated using the current $I^2$ index formula, as described by Kasab-Bachi et al. [19] and the proposed $I^2$ index formula, as described above. However, as the proposed changes to the lesion scoring systems for necrotic enteritis, *E. necatrix*, proventriculitis, *E. brunetti*, and microscopic *E. maxima* $I^2$ index had not been implemented in the field, at the time of this analysis, a number of assumptions were required in order to calculate the proposed $I^2$ index.

In order to calculate the proposed $I^2$ index, the scores of the conditions with updated lesion scoring systems (e.g., necrotic enteritis, *E. necatrix*, proventriculitis, *E. brunetti*, and microscopic *E. maxima*) were multiplied by a scaling factor to scale the scores to the new proposed maximum score (available as Supplementary Material upon request). As the dataset contained average scores per flock for each condition, it was not possible to determine how many birds were necropsied and what each individual bird’s lesion scores were for each condition. Therefore, scaling the current scores by the proposed maximum provided the best method to accurately estimate what the proposed $I^2$ scores would likely be, based on the proposed scoring methods.

2.5. Evaluating the Relationships between the Proposed $I^2$ Index and Each of the Performance Parameters

The statistical relationships between the proposed $I^2$ index and each of the four performance parameters, i.e., ADG, FCR, EPEF and percent livability were examined. These analyses were similar to those previously conducted by Kasab-Bachi et al. [19] on this same dataset using the current $I^2$ index. For all statistical models, a type I error rate of 5% and a type II error rate of 20% were used. Four separate multivariable mixed effects linear regression models were built using one performance parameter as the outcome for each model. These data had an inherent nested structure due to a lack of independence between observations, as flocks from the same farm and company would be more similar than those from other farms or other companies due to various management, seasonal, and biological factors. Therefore, a fixed effect was used to control for clustering at the company level, and a random effect was used to control for clustering at the farm level.

For each multivariable model, linearity between the performance parameter and the proposed $I^2$ index was assessed visually using a locally weighted smoother. If the assumption of linearity was violated and the relationship between the performance parameter and the proposed $I^2$ index was identified to be curvilinear, a quadratic term was introduced into the model to meet the assumption of linearity. The assumption of normality was examined visually for both the main and random effects in the model using a normal quantile plot of the standardized residuals and the best linear unbiased predictors (BLUPS), respectively. The assumption of homogeneity of variance was also examined visually by examining a scatter plot of the BLUPS and standardized residuals against the predicted outcome. The standard residuals at the farm level were assessed for the purpose of identifying outliers. Outliers were subsequently examined for recording errors and unique characteristics. All outliers were kept in the final models in an attempt to increase the generalizability of the models.

For ease of interpretation, predicted margins plots with corresponding 95% confidence intervals were generated for statistical models with significant quadratic terms to graphically demonstrate the relationships between each of the various performance parameters and the proposed $I^2$ score.
2.6. Comparison of the Predictive Ability of the Proposed $I^2$ Index Compared to the Current $I^2$ Index

In order to determine which version of the $I^2$ index (i.e., current vs. proposed) was superior at explaining the four production parameters, a model selection approach, commonly employed in the field of economics, was used. This approach was chosen as it begins with a given set of pre-determined models and has the aim of choosing the most favorable model for decision making [21]. As the models were non-nested in nature, the following three common methods for non-nested models were employed: J-test for non-nested models [22], Cox–Pesaran test for non-nested models [23], and the encompass method [24]. The J-test compares the two models by artificially nesting the two models being compared by generating a “comprehensive” artificial model [21,22]. The Cox–Pesaran test uses each model as the null hypothesis, and then the two models’ predictive abilities are compared against one another [21,23]. The encompass method asks the question, “Can the first model explain one or more features of the rival model?” in order to determine which model is better at predicting the outcome. When all of the features of the rival model can be explained by the first model, it is assumed that the first model encompasses the rival model, and therefore is significantly better than the rival model at predicting the outcome [21,24]. However, if this is not the case, then, it is suggested that one model is not significantly better at predicting the outcome than the other model.

In order to perform the J-test and Cox–Pesaran tests for non-nested models, separate multivariable models, including a fixed effect for company, were generated for each production parameter using the current $I^2$ index and the proposed $I^2$ index separately as the explanatory variables. The random effect of farm level was excluded from these models, as it was not possible to compare models with random effects using these methods [21]. In order to employ the encompass method for model selection, multivariable mixed effects linear regression models controlling for both company location and farm using fixed and random effects, respectively, were subsequently built for each of the production parameters and each model included both the proposed and current $I^2$ indices as predictor variables.

3. Statistical Software

All data management, descriptive statistical analyses, and graphical visualizations of the data were performed using Stata 14® for Windows (Stata Corporation, College Station, TX, USA) and Microsoft Excel for Windows (Microsoft, Redmond, WA, USA).

The implementation of the proposed changes to the $I^2$ index provided greater variation in $I^2$ scores at the flock level as compared with the current $I^2$ index, as demonstrated by a larger deviation and range of $I^2$ scores (Table 2). In addition, both the current and proposed $I^2$ index did not result in any flocks with negative scores (Table 2).

Table 2. Descriptive statistics for flock level $I^2$ scores calculated using the current and proposed $I^2$ indices.

| $I^2$ Index | Min | Max | Mean | Standard Deviation | Number of Flocks with a Negative Score |
|-------------|-----|-----|------|--------------------|---------------------------------------|
| Current     | 48.2| 100 | 95.6 | 3.83               | 0                                     |
| Proposed    | 9   | 100 | 93.8 | 5.96               | 0                                     |

The proposed $I^2$ index was found to have statistically significant relationships with all four of the poultry parameters examined (Table 3). The proposed $I^2$ index demonstrated a significant positive relationship with both ADG and EPEF (Table 3). Conversely, the proposed $I^2$ index demonstrated a significant negative relationship with FCR (Table 3). The proposed $I^2$ index was found to have a significant curvilinear (i.e., quadratic) relationship with percent livability (Table 3 and Figure 1). As the proposed $I^2$ score increased, percent livability was found to increase until a maximum livability of 95% at an $I^2$ score of 84, and then leveled off until a maximum $I^2$ score of 100 was reached (Figure 1). However, it is important to note that the confidence intervals for the predicted margins within the $I^2$
range of 9 to 60 are quite large, due to a small number of observations in this range. On the basis of visual assessment the BLUPS and standardized residuals for all mixed effects multivariable models met the assumptions of normality and homogeneity of variance. There were also no concerning residuals or potential outliers identified by a visual assessment of the standardized residuals and BLUPS.

When examining if the proposed or the current $I^2$ index was superior at predicting the various performance parameters, the results varied by both production parameter and by statistical test employed (Table 4). Overall, neither the current $I^2$ index nor the proposed $I^2$ were significantly better than the other at predicting feed conversion ratio (Table 4). The proposed $I^2$ index was found to be superior at predicting percent livability as compared with the current $I^2$ index based on the results from the J- and Cox–Pesaran tests (Table 4). However, these results were contradicted by the encompass method which indicated that neither method was significantly better than the other at predicting percent livability (Table 4). On the basis of the results from the encompass method, the proposed $I^2$ index was found to be superior to the current $I^2$ index at predicting ADG, however, the J- and Cox–Pesaran tests suggested that neither index was superior as compared with the other (Table 4). Finally, the proposed $I^2$ index was found to be superior at predicting EPEF according to the J-test and the encompass method, however, it was not found to be significantly better than the current $I^2$ index when the Cox–Pesaran test was employed (Table 4).

![Graph](image_url)
Table 3. Flock level descriptive statistics for untransformed outcome variables and significant results of mixed effect linear regression models examining the relationships between the proposed $I^2$ index and each of the four key performance indicators.

| Performance Parameter (Outcome) | Number of Flocks | Performance Parameter Descriptive Statistics | Proposed $I^2$ Score $\beta$ | 95% CI | $p$-Value |
|---------------------------------|------------------|---------------------------------------------|-------------------------------|--------|-----------|
|                                 |                  | Mean | Min  | Max | 0.038 | 0.023, 0.053 | <0.001 |
| Average daily gain (g)          | 3590             | 54.30 ± 4.59 | 38.00 | 72.58 | 0.038 | 0.023, 0.053 | <0.001 |
| Feed conversion ratio           | 3590             | 1.76 ± 0.11 | 1.41 | 2.31 | −0.0012 | −0.00082, −0.0015 | <0.001 |
| Percent livability (%)          | 3590             | 95.20 ± 2.76 | 66.99 | 100 | 0.13 | 0.042, 0.22 | 0.004 |
|                                 |                  |                  | 0.00079 | 0.00026, 0.0013 | 0.003 |
| European efficiency factor      | 3590             | 294.08 ± 27.05 | 162.00 | 386.57 | 0.42 | 0.26, 0.54 | <0.001 |
| Average daily gain (g)          | 3590             | 54.30 ± 4.59 | 38.00 | 72.58 | 0.038 | 0.023, 0.053 | <0.001 |
Table 4. Results of three different statistical tests (J-Test, Cox–Pesaran Test, and encompass method) indicating if the proposed $I^2$ index, current $I^2$ index, or neither were superior.

| Performance Parameter                  | J-Test       | Cox–Pesaran Test | Encompass Method |
|----------------------------------------|--------------|------------------|------------------|
| Average daily gain (g)                 | Neither      | Neither          | Proposed $I^2$   |
| Feed conversion ratio                  | Neither      | Neither          | Neither          |
| Percent livability (%)                 | Proposed $I^2$ | Proposed $I^2$  | Neither          |
| European production efficiency factor  | Proposed $I^2$ | Neither          | Proposed $I^2$   |

4. Discussion

The results presented in this study represent an emerging and innovative platform process using an integrated stakeholder evidence-based data-driven framework that focuses on poultry sustainability through linking important intestinal diseases to production measures via the use of a comprehensive numerical index ($I^2$). To the best of the authors’ knowledge, the $I^2$ index is the first comprehensive index that has been developed to assess the overall intestinal health of poultry, and which has been demonstrated to correlate with key performance parameters in broiler production. This approach is valuable as a producer-friendly means of assessing the overall intestinal health of flocks and allows for opportunities for producers to make informed decisions with regards to implementing potential interventions to improve the intestinal health of their flocks. Further adoption and utilization of this intestinal integrity index by the industry could be an effective additional step towards sustainable commercial poultry production; improvements to intestinal health could increase flock performance, welfare, and profitability. The HTSi system and the $I^2$ index have been adopted by Elanco customers in over 62 countries to date, indicating the practicality of using this surveillance approach to monitor trends and patterns of intestinal diseases globally over time. Due to the global scope of this system, the HTSi database contains an immense amount of data that can be used for benchmarking across flocks, production flows, and geographic regions. Currently there is wide geographic variation in the difference between observed livestock productivity and the best that can be achieved, based on current genetic material and technology, this is termed the “yield gap” [2]. The $I^2$ index, combined with information contained in the HTSi database, could be used to identify these yield gaps in production and suggest possible interventions to close these gaps, in order to further drive sustainable commercial production of chicken. This could be especially useful in newly expanding markets, such as South Africa and China [2,11].

According to the current $I^2$ index, many flocks would be concentrated within a relatively narrow range of $I^2$ index scores (95–100) but in some cases showed marked differences in productivity measures. Consequently, Elanco Animal Health have expressed an interest in exploring whether increasing the variability of the $I^2$ index scores could help explain productivity differences between flocks. Therefore, the results of this study are promising, as it was found that the proposed $I^2$ index produced a greater range and increased variation in $I^2$ index scores at the flock level as compared with the current $I^2$ index, without resulting in flocks with negative $I^2$ index scores.

The proposed $I^2$ index was found to have statistically significant positive relationships with ADG and EPEF, and a statistically significant negative relationship with FCR based on multivariable linear regression analysis. These results concur with previous results by Kasab-Bachi et al. [19] who found positive statistical associations between the current $I^2$ index and each of these three production parameters. These findings are not surprising, as the $I^2$ index is comprised of intestinal conditions that reflect pathogenic invasion of the intestinal system, which results in decreased feed efficiency and increased demand for resources in order for the affected birds to reach a target market weight [13,25,26]. The positive associations between each of these production parameters and the proposed $I^2$ index suggests that the proposed $I^2$ index could be an effective tool for linking intestinal health to production metrics.

The proposed $I^2$ index was also found to have a statistically significant quadratic relationship with percent livability based on multivariable analyses. Overall percent livability was found to increase until
a maximum livability of 95% at a proposed $I^2$ index score of 84 and leveled off with increasing $I^2$ index scores. This was in contrast to work previously completed by Kasab-Bachi et al. [19], who did not find a significant statistical association between the current $I^2$ index and percent livability. The difference in the predictive ability of the two $I^2$ index scores is likely due to differences in the schemes used to weight the individual conditions, as the proposed $I^2$ index weights the intestinal conditions based on significant associations found between the $I^2$ index and each of the performance metrics, as well as the economic impact and pathogenicity of each condition [19].

As previously discussed, the current $I^2$ index has been found to be an effective predictor of ADG, FCR, and EPEF, however, the current $I^2$ index has been found to not effectively predict percent livability [19]. These findings drove proposed changes to the $I^2$ index in order to improve the predictive performance of the index, as previously mentioned. As a result of these proposed changes, the proposed $I^2$ index was found to be significantly statistically associated with all four production parameters, including percent livability, which was not found to be associated with the current $I^2$ index [19]. When comparing the predictive performance of the proposed $I^2$ index compared to the current $I^2$ index, based on three statistical tests for non-nested models (e.g., J-test, Cox–Pesaran test, and the encompass method), the results suggested that the proposed $I^2$ index was at least as effective at predicting the four performance outcomes as the current $I^2$ index. Furthermore, it was also suggested by at least one statistical test of the three, that the proposed $I^2$ index was superior to the current $I^2$ index for predicting percent livability, ADG, and EPEF. The discrepancies between the statistical tests are likely a result of the impact of clustering at the farm level; the encompass method was the only method that was able to control for this level of clustering via the use of a random effect. These changes to predictive performance of the $I^2$ index demonstrate the value of using a data-driven approach when developing and improving health metrics and tools. Furthermore, the authors suggest the adoption of the proposed $I^2$ index in practice, due to the improved predictive performance.

When interpreting the results of this study, it is important to consider that a number of assumptions were required in order to calculate the proposed $I^2$ index scores for all analyses. The proposed changes to the lesion scoring systems for necrotic enteritis, *E. necatrix*, proventriculitis, *E. brunetti*, and microscopic *E. maxima* were not implemented in the field at the time these analyses were carried out. It is possible that the assumption used to assign new scores to these conditions based on the proposed changes to the respective lesion scoring systems did not truly represent what scores would have been assigned in the field. As a result, the descriptive statistics generated for the proposed $I^2$ index scores are approximations. However, it is unlikely that these assumptions would have a large impact on the calculated $I^2$ index scores, as these conditions represent only five of the 23 intestinal conditions captured within this index. Moreover, only two of these conditions, *E. brunetti* and *E. necatrix*, were assigned heavier condition weights in the proposed $I^2$ index formula, +8 and +12 respectively. However, as there were no positive reports of *E. brunetti* in the dataset, it is reasonable to assume that the impact of the assumptions for these conditions was minimal. Therefore, it is likely that the calculated proposed $I^2$ index scores are adequate approximations of $I^2$ index scores that would be seen in the field if the proposed changes to the condition scoring systems had been implemented. An analysis of the impact of the lesion scoring systems on the calculated $I^2$ index scores, once they have been implemented in the field, is warranted in order to further validate this surveillance tool.

Additionally, it is possible that misclassification bias could be of concern for this study, if the intestinal conditions used to calculate the $I^2$ index were misdiagnosed. This is of particular concern, as any misclassification errors would likely be further impacted by the assumptions used to calculate the proposed $I^2$ index scores. However, misclassification was likely minimal as data collection for HTSi is extremely systematic and the individuals who perform the necropsies are extensively trained and utilize a standard reference guide to score conditions [20]. Furthermore, if misclassification occurred it would likely be non-differential in nature, as the misclassification of lesion scores would likely not be associated with performance, thereby biasing the results towards the null. This would strengthen our conclusion that there was a significant association between the $I^2$ scores and performance.
parameters, as the identified statistical associations would likely be weaker than what is truly the case, if non-differential misclassification bias is present.

It has been well acknowledged that surveillance systems are only as good as their population coverage. Due to the extensive global coverage of HTSi, the HTSi database represents a unique and comprehensive source of data that can be used to monitor intestinal health and performance in commercial poultry flocks globally. Thus, widespread industry use of this platform in conjunction with the I² index to make informed management decisions that impact productivity could be an additional step towards sustainable production. However, performance metrics are currently only captured in HTSi for a small subset of producers and geographic regions. As a result, for the analyses presented in this paper, performance metrics were only available for 10 production flows and a limited number of flocks within the USA and the UK. Although the study flocks are representative of the industry average in these two countries (i.e., in terms of production styles, feeding programs, genetics, etc.), there was limited variation in production types and management factors among the study flocks. Consequently, extrapolating the results of this study to other populations may not be appropriate, due to geographic differences in production styles, management styles, bird health, and pathogen prevalence and challenges. In order to further validate the use of the I² index as a means to predict performance, and hence drive sustainability, a more comprehensive analysis using information from a wider diversity of flocks (e.g., production styles, genetics, feeding programs, geographic locations) is warranted.

5. Conclusions

In conclusion, the HTSi database and the proposed I² index are valuable tools which can be used to monitor performance, evaluate intervention, and treatments, as well as identify evidence-based solutions to complex issues facing the poultry industry. Therefore, adoption of these tools by producers and, subsequently, the commercial poultry industry as a whole represents an important tool that can also be used to support, inform, and evaluate other concurrent industry efforts to drive economic sustainability and profitability for the poultry industry globally. Once the proposed updates to the lesion scoring systems have been implemented in the field, the I² index should be examined once again to identify further opportunities for improvement. Our results demonstrate the adaptive ability of this platform approach to global surveillance of poultry intestinal health and highlight the strength of data-driven approaches in the development and improvement of comprehensive health metrics, such as the I² index. In the future, similar comprehensive health indices could be applied to other animal production systems in order to further drive sustainable food production in a more comprehensive and integrated manner.

**Author Contributions:** This paper was conceptualized by J.B.W. Formal analysis and writing were undertook by A.L.S. and the original draft was done by H.K.-B. Review and editing was done by J.R. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research was funded by Elanco Animal Health.

**Acknowledgments:** The authors would like to thank Elanco Animal Health for providing the data used in this analysis and funding for the project, as well as Kim Levere from the University of Guelph for her assistance in developing the lesion normalization scheme. Finally, to Tara Roberts for her contributions for project management and formal analysis.

**Conflicts of Interest:** The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.
References

1. Reaping the Benefits: Science and the Sustainable Intensification of Global Agriculture. Available online: http://royalsociety.org/Reapingthebenefits (accessed on 4 January 2018).
2. Godfray, H.C.J.; Beddington, J.R.; Crute, I.R.; Haddad, L.; Lawrence, D.; Muir, J.F.; Pretty, J.; Robinson, S.; Thomas, S.M.; Toulmin, C. Food security: The challenge of feeding 9 billion people. *Science* 2010, 327, 812–818. [CrossRef] [PubMed]
3. Pelletier, N.; Tydemers, P. Forecasting potential global environmental costs of livestock production 2000–2050. *Proc. Natl. Acad. Sci. USA* 2010, 107, 18371–18374. [CrossRef] [PubMed]
4. FAOSTAT. Available online: http://faostat.fao.org/default.aspx (accessed on 27 December 2017).
5. Foley, J.A.; Ramankutty, N.; Brauman, K.A.; Cassidy, E.S.; Gerber, J.S.; Johnston, M.; Mueller, N.D.; O’Connell, C.; Ray, D.K.; West, P.C.; et al. Solutions for a cultivated planet. *Nature* 2011, 478, 337–342. [CrossRef] [PubMed]
6. Perez, A.M. Past, present, and future of veterinary epidemiology and economics: One health, many challenges, no silver bullets. *Front. Vet. Sci.* 2015, 2, 1–4. [CrossRef] [PubMed]
7. Vaarst, M.; Steenfeldt, S.; Horsted, K. Sustainable development perspectives of poultry production. *Worlds Poult. Sci. J.* 2015, 71, 609–620. [CrossRef]
8. Schwabe, C. *Veterinary Medicine and Human Health*, 3rd ed.; Williams and Wilkins: Baltimore, MD, USA, 1964.
9. Briault, A. Economic and one health. *Vet. Rec.* 2014, 174, 283. [CrossRef] [PubMed]
10. Dharne, H.V. Maintaining Gut Integrity. *Poult. Site*. 2008. Available online: http://www.thepoultrysite.com/articles/978/maintaining-gut-integrity/ (accessed on 1 January 2018).
11. Blake, D.; Tomley, F. Parasites ramble on: Focus on food security securing poultry production from the ever-present *Eimeria* challenge. *Trends Parasitol.* 2014, 20, 12–19. [CrossRef] [PubMed]
12. Van Immerseel, F.; Rood, J.; Moore, R.J.; Titball, R.W. Rethinking our understanding of the pathogenesis of necrotic enteritis in chickens. *Trends Microbiol.* 2009, 17, 32–36. [CrossRef] [PubMed]
13. Timbermont, L.; Haesebrouck, F.; Ducatelle, R.; Van Immerseel, F. Necrotic enteritis in broilers: An updated review on the pathogenesis. *Avian Pathol.* 2011, 40, 341–347. [CrossRef] [PubMed]
14. Shojadoost, B.; Vince, A.R.; Prescott, J.F. The successful experimental induction of necrotic enteritis in chickens by *Clostridium perfringens*: A critical review. *Vet. Res.* 2012, 43, 74. [CrossRef] [PubMed]
15. Cervantes, H.M. Antibiotic-free poultry production: Is it sustainable? *J. Appl. Poult. Res.* 2015, 24, 91–97. [CrossRef]
16. De Gussem, M. Coccidiosis in poultry: Review on diagnosis, control, prevention and interaction with overall gut health. In Proceedings of the 16th European Symposium on Poultry Nutrition, Strasbourg, France, 26–30 August 2007; pp. 253–261.
17. Skinner, J.T.; Bauer, S.; Young, V.; Pauling, G.; Wilson, J. An economic analysis of the impact of subclinical (mild) necrotic enteritis in broiler chickens. *Avian Dis.* 2010, 54, 1237–1240. [CrossRef] [PubMed]
18. Zhang, J.J.; Wang, L.X.; Ruan, W.K.; An, J. Investigation into the prevalence of coccidiosis and maduramycin drug resistance in chickens in China. *Vet. Parasitol.* 2013, 191, 29–34. [CrossRef]
19. Kasab-Bachi, H.; Arruda, A.G.; Roberts, T.E.; Wilson, J.B. 2017. The use of large databases to inform the development of an intestinal scoring system for the poultry industry. *Prev. Vet. Med.* 2013, 146, 130–135. [CrossRef]
20. *Elanco Animal Health, 2010 Broiler Disease Reference Guide*; Elanco Animal Health: Greenfield, IN, USA, 2010.
21. Pesaran, H.; Weeks, M. Non-nested hypothesis testing: An overview. In *A Companion to Theoretical Economics*; Baltagi, B.H., Ed.; Blackwell Publishing Ltd.: Malden, MA, USA, 2003; pp. 279–309.
22. Davidson, R.; MacKinnon, J. Several tests for model specification in the presence of alternative hypotheses. *Econometrica* 1981, 49, 781–793. [CrossRef]
23. Cox, D. Further results on tests of separate families of hypotheses. *J. R. Stat. Soc.* 1962, B24, 406–434. [CrossRef]
24. Mizon, G.E.; Richard, J.F. The encompassing principle and its application to non-nested hypotheses. *Econometrica* 1986, 54, 657–678. [CrossRef]
25. Cravens, R.L.; Goss, G.R.; Chi, F.; De Boer, E.D.; Davis, S.W.; Hendrix, S.M.; Richardson, J.A.; Johnston, S.L. The effects of necrotic enteritis, aflatoxin B1, and virginiamycin on growth performance necrotic enteritis lesion scores, and mortality in young broilers. *Poult. Sci.* **2013**, *92*, 1997–2004. [CrossRef] [PubMed]

26. M’Sadeq, S.; Wu, S.; Swick, R.A.; Choc, M. Towards the control of necrotic enteritis in broiler chickens with in-feed antibiotics phasing-out worldwide. *Anim. Nutr.* **2015**, *1*, 1–11. [CrossRef] [PubMed]

© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).