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Two applications are described of a hierarchical model that can express uncertainty regarding a pre-specified monotonicity hypothesis for binomial probabilities. The results relate to time series with possibly monotonic success rates, isotonic regression, and the evaluation of performance indicators. The model can alternatively be interpreted as a random effects over-dispersion formulation for beta-binomial observations, within which the population proportions definitely satisfy a monotonicity specification. Practical ways of choosing the prior parameters for a Bayesian analysis are recommended. The primary application relates to a study of early hematopoiesis, and revisits a time series of proportions of masked progenitor cells from the bone marrow of a hybrid safari cat. The data for this cat are shown to be reasonably consistent with an assumption of strictly decreasing population proportions. The experimental outcomes for the other cats in the study are reviewed. An introductory application results from a Veterans' Administration hospital quality monitor, and concerns the failure to return rates for psychiatric patients attending substance abuse clinics. While smoothed performance indicators are devised, estimated standard errors of the corresponding sample proportions, which measure their extra-binomial sampling variation, are also calculated.

KEY WORDS: binomial, beta-binomial, monotonicity, Bayesian hierarchical model, over-dispersion, random effects model, early hematopoiesis, substance abuse, quality monitoring, performance indicators, isotonic regression, time series.

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1. INTRODUCTION

When investigating m population proportions $\theta_1, \theta_2, \ldots, \theta_m$ it is sometimes appropriate to consider monotonicity constraints

$$\theta_1 \leq \theta_2 \leq \ldots \leq \theta_m \quad , \tag{1.1}$$

based upon prior reasoning. The θ_i might for example represent the true success rates for a treatment, at consecutive time periods, where the success rates are thought to be non-decreasing in time. They may alternatively denote the success rates for m multi-centered trials, where the centers have been ordered according to preliminary performance indicators. More generally, we may have an isotonic regression situation where the θ_i are thought to possess the same ordering as an increasing covariate, e.g., dose level.

A major theme of this paper lies in the argument that, while there may be some prior justification for the monotonicity constraints (1.1), the previous information may be insufficient to assume that (1.1) definitely holds. In section 3, hierarchical assumptions are introduced which, under binomial sampling assumptions, relax the investigator's prior belief in (1.1), thus permitting the observed data to refute (1.1). The probability model described may alternatively be interpreted as a random effects model for beta-binomial observations. The embedded extra-binomial variation then yields potentially quite different conclusions regarding the proposed monotonicity of the population proportions.

2. TWO DATA SETS

2.1 The Veterans' Administration hospital quality monitor data

We analyze part of a data set modeled by West and Aguilar (1997), Aguilar and West (1998), West et al. (1998), and Burgess et al. (2000), using Bayesian multiple time series. The subsample considered here provides information from the years 1992 and 1993 for $m = 159$ hospitals in the Veterans' Administration (VA) system. The 1993 data provide our dependent variables, and the 1992 data are used to calculate a set of explanatory variables.

Let y_i denote the number of individuals who failed to return for an outpatient visit within 30 days of discharge during 1993 out of the total number of annual discharges at the ith hospital, for $i = 1, 2, \ldots, m$. Then $p_i = y_i/n_i$ can be regarded as a performance indicator or measure of (lack of) quality for the ith hospital. The sample sizes range from 5 to 1142 with an average of $\bar{n} = 324.7$. Let x_i denote the corresponding proportion for the year 1992. For

our first analysis, we attach our indices after reordering the hospitals according to increasing values $x_1 < x_2 < \cdots < x_m$. The rank ordering of the performance indicators for 1992 is thus taken into account when considering the rank ordering for 1993. Assumptions of monotonic increasing population proportions for 1993, under binomial or beta-binomial assumptions for the y_i, will be investigated in section 9.

(Figure 1 is about here)

The association between the raw performance indicators is described by the entries to the scatterplot in Figure 1, which plot the p_i against the x_i. There is some overall increasing trend, but with considerable random scatter. The hospitals' raw performance indicators for 1992 do not provide good predictions of the performances for 1993. The solid plot describes a piecewise linear isotonic regression, as defined in sections 4.3 and 9, and justified under beta-binomial sampling assumptions. The abscissa of this plot provide smoothed performance indicators for 1993 which are consistent with the rank ordering for 1992. The dotted plots add or subtract estimated standard errors of the 1993 sample proportions, which account for substantial extra-binomial variation. The magnitudes of the estimated standard errors provide guidance regarding the usefulness of the fitted performance indicators, for predictive rather than descriptive purposes. Further discussion is provided in section 9.

(Figure 2 is about here)

The preceding explanatory variables may be replaced by the VA's diagnostic related group (DRG) predictions that, for each hospital in each year, are supposed to provide predictions of the corresponding p_i. The DRG predictions for 1993 do not depend upon the sample proportions for years prior to 1993. In Figure 2, the p_i are plotted against the DRG predictions. The performances of these predictions and the previous raw performance indicators are comparable. As the labeling of the x-axis of Figure 2 is quite compressed, when compared with Figure 1, the fitted isotonic graph, while similar in shape, represents a much steeper regression. The estimated standard errors of the corresponding sample proportions are however comparable.

In other analyses, not reported here, the explanatory variables were replaced by equally weighted or unequally weighted combinations of appropriately normalized proportions for 1992 and DRG predictions for 1993. Quite surprisingly, none of these combinations yielded

substantive modifications to the shape of the isotonic regression graph, and the estimated standard errors were at best only marginally reduced. The inclusion of multiplicative interaction terms failed to improve the predictive performance.

2.2 A Time Series for a Safari Cat

The data in Table 1 comprise an important subset of the early hematopoiesis data analyzed by Newton et al. (1995) using a finite Markov Chain model with a formulation based upon biomedical considerations and relating to earlier work by Guttorp et al. (1990) and Abkowitz et al. (1990, 1993). The bone marrow of humans and other vertebrates contains a relatively small number of remarkable cells, the hematopoiesis stem cells. Hematopoiesis is the complex dynamic process that maintains this population; see Brecher et al. (1986), Golde (1991), and Lemischka (1992). A thorough discussion of early hematopoiesis is provided by Newton et al. They refer to a standard theory where the entire supply of stem cells is actively dividing, and Kay's (1965) theory of clonal succession, which hypothesizes that most stem cells are inactive, and that at any time a small proportion are proliferating. A variety of alternative sets of biomedical assumptions are available. The studies are of current clinical relevance to cancer treatments, bone marrow transplantation and gene transfer methods. See also Abkowitz et al. (1998, 2002).

(Table 1 is about here)

Newton et al. describe experiments by Janis Abkowitz and her colleagues at the University of Washington, e.g., Abkowitz et al. (1988), where numbers of domestic type cells in samples of progenitor cells are recorded at different sample times for a number of cats. The second column of Table 1 records the $m = 18$ unequally spaced sampling times (t_i) for their cat with id 40665. This is one of the six cats considered by Newton et al. who were subjected to a bone marrow transplantation treatment. The third and fourth columns record the corresponding observed numbers of domestic type cells y_i and the number of progenitor cells n_i. The observed proportions p_i and associated estimated standard errors s_i are described in the fifth and sixth columns.

Let θ_i denote the proportion of domestic-type cells in the full progenitor pool at time t_i, and assume that y_i is the numerical realization of a random variable Y_i. In their section 4.2, Newton et al. show that, subject to their modeling specifications, and with the proportion of domestic-type cells in a stem cell compartment assumed constant over time, it is reasonable

to take the counts Y_i to be conditionally independent and binomially distributed with $Y_i|\theta_i \sim \text{BIN}(\theta_i, n_i)$, for $i = 1, 2, \ldots, 18$. Our own, now monotonic decreasing, hypothesis $\theta_1 \geq \theta_2 \geq \cdots \geq \theta_{18}$ may or may not concur with any particular specialized biomedical theory for early hematopoiesis. However the analyses of sections 6, 7, and 8 will suggest that, even under strict binomial sampling assumptions, our hypothesis should not be entirely refuted. A specially formulated tail probability of about 14% is reported. Any reasonable relaxation of the binomial assumptions would probably lessen the evidence against the hypothesis. In their section 8.2, Newton et al. discuss modeling conditions under which extra-binomial sampling assumptions are more appropriate. In order to justify a binomial model by random sampling rather than theoretical assumption, we would firstly seek to fully define a reference population or sampling frame. It would seem necessary to effectively distinguish all cells in the full progenitor pool. Newton et al. describe the actual experimental sampling mechanism in their section 2.

The entries in the last column of Table 1 provide a preliminary data analysis for cat 40665. These two sample binomial test statistics may be used to test the hypotheses that $\theta_i > \theta_{i+1}$, for $i = 1, 2, \ldots, 17$, on an individual basis. For example, the high positive value $z_{16} = 3.178$ attaches apparently strong statistical significance in favor of the conclusion that $\theta_{16} > \theta_{17}$. The only apparently significant evidence against our monotonic decreasing hypothesis is provided by the negative values $z_{15} = -1.786$ and $z_5 = -2.635$, which relate to the high values $p_{16} = 0.482$ and $p_6 = 0.789$ for the subsequent sample proportions.

Our main analysis for cat 40665 will however suggest that the population proportions may well be noticeably strictly decreasing, under extra-binomial sampling assumptions. Of the other cats in the treatment group, cats 40005a, 40006, and 40823 also yielded experimental outcomes consistent with this property. The data for cat 40004 do not appear to possess any special features. The fragmented data for cat 40005b require further biomedical explanation. It is difficult to fairly compare the treatment and control groups, since much of the data for the five control cats were recorded at substantially higher time points. However, there is some suggestion of slightly decreasing population proportions for cats 63458 and 63133, and negligible evidence for cats 63122, 63144, and 65044. Any applied appraisal of the entire data set considered by Newton et al. might quite reasonably suggest that the data do not contain the type of information which is likely to support or distinguish between extremely sophisticated hypotheses or clinical interpretations. Apparent features in the data may

instead be explainable by overdispersion, perhaps of an even more complex nature than indicated by a beta-binomial sampling model (see Hsu et al. 1991). The bootstrap analysis by Newton et al. (section 6) should be considered in this context.

3. A HIERARCHICAL MODEL

A four stage probability model with the following first two stages is employed:
Stage 1: Observations $Y_1, Y_2, \ldots, Y_m$ are independent and binomially distributed, given $\theta_1, \theta_2, \ldots, \theta_m$, with $Y_i|\theta_i \sim \text{BIN}(\theta_i, n_i)$, for $i = 1, 2, \ldots, m$.
Stage 2: The θ_i are independent and beta distributed, given an unknown parameter γ and respective conditional means ξ_i where, with the standard parameterization, $\theta_i|\gamma, \xi_i \sim \text{Beta}\{\gamma\xi_i, \gamma(1-\xi_i)\}$, for $i = 1, 2, \ldots, m$.

With the further assumption that the unknown ξ_i satisfy the monotonicity specification

$$\xi_1 \leq \xi_2 \leq \cdots \leq \xi_m \quad , \tag{3.1}$$

the preceding two stages can be interpreted in either of the following two ways:
(A) Let Stage 1 represent the sampling distribution of the Y_i and Stage 2 describe the first stage of a hierarchical prior distribution for the population proportions θ_i (further stages for γ and the conditional means ξ_i will be added below). In this case Stage 2 represents uncertainty in the belief that the monotonicity hypothesis (1.1) holds for the θ_i, thus extending an idea introduced by O'Hagan and Leonard (1976) in a single parameter normal situation. For given ξ_i and γ, the parameter θ_i can be said to possess a beta distribution with mean ξ_i and sample size γ, where this (prior) sample size measures the degree of belief in (1.1). As $\gamma \to \infty$ the monotonicity constraints are completely specified for the θ_i. A small value of γ represents substantial uncertainty in this hypothesis. Our formulation does not however require the specification of a definite value for γ, since the current data will typically provide considerable information regarding γ.
(B) The two stages may alternatively be combined. Unconditionally on θ_i, Y_i possesses a beta-binomial distribution, labeled by its parameters ξ_i and γ, and sample size n_i. The probability mass function of Y_i, given ξ_i and γ, is

$$p(Y_i = y_i|\xi_i, \gamma) = {}^{n_i}C_{y_i} l_i^*(\xi_i, \gamma) \quad , \tag{3.2}$$

for $y_i = 0, 1, \ldots, n_i$, with ${}^{n_i}C_{y_i} = n_i!/y_i!(n_i - y_i)!$ and

$$l_i^*(\xi_i, \gamma) = \frac{B\{\gamma\xi_i + y_i, \gamma(1-\xi_i) + n_i - y_i\}}{B\{\gamma\xi_i, \gamma(1-\xi_i)\}} \quad , \tag{3.3}$$

where $B(a_0, a_1) = \Gamma(a_0 + a_1)/\Gamma(a_0)\Gamma(a_1)$ is the complete beta function with arguments a_0 and a_1. With the ξ_i now denoting our population proportions, we have a conditionally independent beta-binomial sampling model, within which the monotonicity specification in (3.1) is definitely satisfied as a modeling assumption. The plausibility of this specification may of course be further investigated.

In either case, the conditional distributions of the θ_i, given γ, the ξ_i and the observed values y_i of the Y_i are, for $i = 1, 2, \ldots, m$, independently beta with respective (posterior) sample sizes $n_i + \gamma$ and means

$$\theta_i^* = \rho_i p_i + (1 - \rho_i)\xi_i \quad , \tag{3.4}$$

where $p_i = y_i/n_i$ and

$$\rho_i = \rho_i(\gamma) = \frac{n_i}{n_i + \gamma} \quad . \tag{3.5}$$

In case (A), (3.4) describes the conditional posterior mean of θ_i. The θ_i^* compromise between the ξ_i satisfying the monotonicity specification (3.1), and the p_i, which can be taken to represent a general alternative hypothesis. Any data-based estimate of the average shrinkage proportion

$$\bar{\rho} = m^{-1} \sum_{i=1}^{m} \rho_i(\gamma) \tag{3.6}$$

can be interpreted as an overall measure, on a unit scale, of the evidence against the monotonicity hypothesis (1.1), and in favor of a general alternative hypothesis. The weighted modifications $\tilde{\rho} = \sum n_i \rho_i / N$ and $\hat{\rho} = \sum (n_i + \gamma)\rho_i / \sum (n_i + \gamma) = N/(N + \gamma)$, with $N = \sum n_i$ are more sensitive to values of the larger n_i. The complicated refinement $\rho^\dagger = \sum \rho_i (p_i - \xi_i)^2 / \sum (p_i - \xi_i)^2$ may be justified by reference to a quadratic loss function.

Under the beta-binomial interpretation (B), the $P_i = Y_i/n_i$ are unbiased estimators of the ξ_i with respective variances $n_i^{-1} D_i \xi_i (1 - \xi_i)$, where $D_i = (n_i + \gamma)/(1 + \gamma)$ is the ith over-dispersion factor. These estimators do not however take account of (3.1). Moreover, not all of the $m+1$ parameters γ and $\xi_1, \xi_2, \ldots, \xi_m$ are identifiable from the data, as there are just m observations. We consequently extend our conditionally independent beta-binomial model, by introducing the following random effects assumption:

Stage 3: Given $b_0 = \lambda\eta$ and $b_1 = \lambda(1 - \eta)$, the ξ_i possess the probability structure of the increasing order statistics based upon a random sample of size m from a Beta(b_0, b_1) distribution i.e. a beta distribution with mean η and sample size λ.

Our random effects beta-binomial sampling model for case (B) possesses just three parameters γ, λ, and η. When m is moderate to large, it is therefore possible to draw sensible proper Bayes inferences regarding these three identifiable parameters, and also for the ξ_i. Posterior estimates for γ and the ξ_i can thereby be imputed for the parameters of the preceding conditionally independent beta-binomial model. For computational convenience, we initially take the distribution of the parameters γ and λ in the prior assessment to be discrete. The prior distribution for the three parameters of our random effects model is selected as follows:

Stage 4: γ, λ, and η are independent, and $\eta \sim \text{Beta}(d_0, d_1)$. The distribution of γ assigns probabilities $\pi_1, \pi_2, \ldots, \pi_k$ to the points $g_1, g_2, \ldots, g_k$, and the distribution of λ assigns probabilities $\delta_1, \delta_2, \ldots, \delta_l$ to the points $h_1, h_2, \ldots, h_l$.

The assumption of prior independence of γ and λ can be relaxed by taking these parameters to possess a general discrete joint distribution on a $k \times l$ dimensional grid. Practical choices of the prior parameters will be discussed in section 5, and, given the sensitivity analysis of section 8, further prior specification does not present quite as many barriers as one might imagine. In a special case it will just be necessary to choose prior estimates n_0 and λ_0 for γ and λ, and, with $d_0 = d_1 = 1$, to then consider the sensitivity of the posterior inferences to the choices of n_0, λ_0, k, and l. Baseline values for n_0 and λ_0 will be recommended. Large values for k and l will yield close approximations to inferences under an interesting thick-tailed continuous prior distribution, which is effectively assumed.

In case (A), Stages 2, 3, and 4 provide a hierarchical prior distribution for the θ_i. Stage 3 permits input from the data regarding the values of the Stage 2 parameters ξ_i. Stage 4 facilitates input from the data regarding the value of γ, and the Stage 3 parameters $b_0 = \lambda\eta$ and $b_1 = \lambda(1-\eta)$. Related hierarchical models for binomial probabilities, without the constraints in (3.1), provide alternatives to the binomial logit/normal prior or normal random effects developments by Leonard (1972, 1976), Warn et al. (2002), and many others.

4. POSTERIOR CONSIDERATIONS

4.1 Posterior Inferences

In case (A) of section 3 the marginal posterior distribution of θ_i averages a beta distribution with sample size $n_i + \gamma$ and mean θ_i^* satisfying (3.4), with respect to the unconditional posterior distribution of γ and the ξ_i. All posterior quantities of interest for both cases (A) and (B) may be calculated, subject to a minor approximation, via standard Metropolis

algorithm/MCMC procedures. See Appendix 2. Unconditional posterior densities can be computed along with the means and standard deviations reported in the current paper.

For illustrative purposes only, note that the posterior distribution of the ξ_i, given γ, λ, and η, may be roughly approximated by taking the ξ_i to possess independent beta distributions, with respective sample sizes $D_i^{-1}n_i + \lambda$ and means

$$\xi_i^* = \frac{D_i^{-1}n_i p_i + \lambda\eta}{D_i^{-1}n_i + \lambda} \quad , \tag{4.1}$$

where $D_i = (n_i + \gamma)/(1 + \gamma)$, but then constraining these distributions to the region defined by (3.1). The expressions in (4.1) constrain the p_i towards a common unknown value η. The posterior means of the ξ_i are furthermore substantially influenced by the constraints in (3.1). As well as taking (3.1) into account, the unconditional posterior inferences create a partial pooling process which roughly speaking has the effect of flattening the ξ_i towards a pooled estimate for η.

When $d_0 = d_1 = 1$, η is estimated by a slightly adjusted center of location of the p_i. For example, the first posterior analysis of section 9, leading to the isotonic regression graph in Figure 1, yielded a posterior mean of 0.439 for η. This compares with the overall sample proportion $p^* = 0.425$, and the average sample proportion $\bar{p} = 0.444$, and accounts, via the shrinkages of the ξ_i, for a flattening of the isotonic regression graph. Pooled information from across the hospitals is thus incorporated. When judging the plausibility of a monotonic relationship, via the residual analysis of sections 6 and 9, it is important to realize that our regression graph meaningfully flattens steeper monotonic graphs which may better fit the data.

4.2 Two Useful Approximations and a Parameter of Interest

In Appendix 1, an approximation to the conditional distribution of the ξ_i, given the θ_i, γ, η, and λ, under Stages 2 and 3 of our probability model is justified unless γ, $b_0 = \lambda\eta$, or $b_1 = \lambda(1 - \eta)$ is small. The approximation constrains m independent beta distributions to the region (3.1). These distributions may, for $i = 1, 2, \ldots, m$, be described as follows:

$$\xi_i|\theta_i, \gamma, \eta, \lambda \sim \text{Beta}\{\tilde{\lambda}\tilde{\xi}_i, \tilde{\lambda}(1 - \tilde{\xi}_i)\} \quad , \tag{4.2}$$

where

$$\tilde{\xi}_i = \zeta\theta_i + (1 - \zeta)\eta \quad , \tag{4.3}$$

and

$$\tilde{\lambda} = \gamma + \lambda + 1 \quad , \tag{4.4}$$

with

$$\zeta = \frac{\gamma + 1}{\gamma + \lambda + 1} \quad . \tag{4.5}$$

This development highlights ζ in (4.5) as an interesting bounded function of γ and λ. As ζ approaches zero, the $\tilde{\xi}_i$ in (4.3) approach the common unknown value η. While the shrinkage proportions ρ_i in (3.5) relate to shrinkages of the θ_i towards the ordered ξ_i, the proportion ζ controls the shrinkages of the $\tilde{\xi}_i$ towards a common value η. Our preceding approximate conditional distribution for the ξ_i provides a key ingredient of the posterior computational procedures described in Appendix 2, and will be made more exact by acceptance sampling. The exact joint distribution of the ξ_i, given the θ_i, γ, η, and λ, initially takes the ξ_i to be independent, with respective densities

$$\tilde{\pi}(\xi_i) \propto \frac{\xi_i^{\eta\lambda - 1}(1 - \xi_i)^{\eta(1-\lambda)-1}\theta_i^{\gamma\xi_i}(1 - \theta_i)^{\gamma(1-\xi_i)}}{B\{\gamma\xi_i, \gamma(1 - \xi_i)\}} \quad , \tag{4.6}$$

for $0 < \xi_i < 1$ and $i = 1, 2, \ldots, m$, but then constrains the joint distribution of the ξ_i to the region (3.1). The acceptance sampling methodology refers to (4.6) without simulating from the corresponding exact distribution. In Appendix 2, the approximation

$$\eta|\boldsymbol{\xi}, \lambda, \mathbf{y} \sim \text{Beta}\{m(\lambda + 1)\bar{\xi} + d_0, m(\lambda + 1)(1 - \bar{\xi}) + d_1\} \tag{4.7}$$

to the conditional posterior (or prior) distribution of η, given the ξ_i and λ, is also motivated, with $\bar{\xi}$ denoting the average ξ_i. The beta distribution in (4.7) possesses sample size $m(\lambda + 1) + d_0 + d_1$, and mean

$$\tilde{\eta} = \frac{m(\lambda + 1)\bar{\xi}}{m(\lambda + 1) + d_0 + d_1} \quad , \tag{4.8}$$

which is close to $\bar{\xi}$ whenever $m(\lambda + 1)$ is large compared with $d_0 + d_1$. The approximation in (4.7) may be contrasted with the exact conditional density

$$\pi(\eta|\boldsymbol{\xi}, \lambda, \mathbf{y}) \propto \pi(\eta)\tilde{l}(\eta, \lambda|\boldsymbol{\xi}) \quad , \tag{4.9}$$

for $0 < \eta < 1$, where $\pi(\eta)$ is a beta density with parameters d_0 and d_1, and

$$\tilde{l}(\eta, \lambda|\boldsymbol{\xi}) = \frac{\prod_{i=1}^{m} \xi_i^{\lambda\eta}(1 - \xi_i)^{\lambda(1-\eta)}}{[B\{\lambda\eta, \lambda(1 - \eta)\}]^m} \quad . \tag{4.10}$$

When justifying (4.7) and (4.10), it is important to note that the information provided about η and λ by fixed ordered values of the ξ_i is the same as when regarding the ξ_i as an

unordered random sample from a beta distribution with mean η and sample size λ. This information is unaffected by knowledge of the data.

4.3 Regression Situations

The methodology underlying the isotonic regression examples of section 2.1 is now discussed. Consider case (B) of section 3, where each Y_i is taken to possess a beta-binomial distribution, conditional on parameters ξ_i and γ. Suppose that each Y_i and corresponding population proportion ξ_i is associated with a pre-specified value x_i of a covariate, where

$$x_1 \leq x_2 \leq \cdots \leq x_m \quad . \tag{4.11}$$

Assume that the ordering in (3.1) of the ξ_i is consistent with the ordering (4.11) of the x_i. A monotonic increasing regression of the ξ_i upon the x_i is therefore assumed. In situations where two or more of the x_i are equal, the ordering of the corresponding ξ_i should be based upon prior specification. Modifications to our procedure, which set two or more of the ξ_i equal, would alternatively be available. The posterior means of the ξ_i under our general analysis may be plotted against the x_i and connected by straight lines. If two or more of the x_i are equal, then the corresponding posterior means may be weighted according to the corresponding sample sizes. The recommended graph provides our estimated isotonic regression of the ξ_i upon the x_i. This semi-parametric approach provides an alternative to parametric procedures (e.g., Leonard and Novick, 1986, and Lee and Nelder, 1996), which replace stages 3 and 4 of our probability model, and the monotonicity assumption (3.1) by the specification of a functional form for the regression of the ξ_i upon the x_i. The precise modeling of this specification might sometimes present practical difficulties.

Our semi-parametric approach is also relevant to case (A) of section 3. If the posterior deviations of the θ_i from the ξ_i, are small, then the preceding estimated isotonic regression of the ξ_i upon the x_i can be used to meaningfully describe a fitted regression of the θ_i upon the x_i. Otherwise it is more important to report posterior inferences for the unconstrained θ_i. This contrasts with previous isotonic regression procedures for binomial data, e.g., Barlow et al. (1972).

While our approach takes into account the ordering of the x_i, the specific values of the x_i are largely ignored in the posterior analysis, though they are re-introduced when plotting the regression of the ξ_i upon the x_i. Many isotonic regression procedures (e.g., Barlow et al. pp. 38 - 40) similarly trade information regarding the x_i for simplicity in the modeling

procedure. Numerous possible adjustments to our method could however be considered. For example, when the regression of the ξ_i upon the x_i is thought to follow a segment of a concave function, (3.1) can be replaced by a decreasing slope specification. Information regarding the x_i can also be incorporated by generalizing Stage 2 of our probability model, by an assumption that $\theta_i|\gamma, \xi_i \sim \text{Beta}\{a_i\gamma\xi_i, a_i\gamma(1-\xi_i)\}$. The a_i adjust the sample size γ and may be specified subjectively as functions of several adjacent x_i. Alternatively beta distributions for increasing ξ_i at Stage 3 may be taken to possess sample sizes λ and means either equal to specified functions of the covariate, or to a hypothesized regression function depending upon the covariate and an unknown parameter vector $\boldsymbol{\beta}$.

4.4 Time Series

Let $\theta_1, \theta_2, \ldots, \theta_m$ denote population proportions corresponding to respective time points $t_1, t_2, \ldots, t_m$ satisfying $t_1 < t_2 < \ldots < t_m$. Then Stages 2 and 3 of our probability model describe a stochastic process for the θ_i with a possibly increasing trend. Stage 1 superimposes conditionally independent binomial variation. More general stochastic processes may be developed by modifying the constraints in (1.1) and (3.1). Monotonic successive differences could for example be considered. When the t_i are unequally spaced they may be regarded as explanatory variables, and the possible generalizations discussed at the end of section 4.3 considered. When the t_i comprise a subset of an equally spaced grid, then the interpolation procedure described in section 7 can instead be employed.

This formulation contrasts with a stochastic growth model where the logits $\alpha_i = \log\theta_i - \log(1-\theta_i)$ satisfy

$$\alpha_i = \alpha_{i-1} + \phi_i + \epsilon_i \quad (i = 1, 2, \ldots, m) \ , \tag{4.12}$$

with

$$\phi_i = \phi_{i-1} + \eta_i \quad (i = 1, 2, \ldots, m) \ , \tag{4.13}$$

where α_0 and ϕ_0 are unknown, and ϵ_i and η_i are independent error terms with zero means and respective common variances V_ϵ and V_η. The formulation in (4.12) and (4.13) parallels a linear growth model for normal means analyzed by West and Harrison (1989, pp. 213-219). The same authors (pp. 562-564) refer to more general models for time-dependent binomial frequencies of this type, which are linear in the logits, with normally distributed error terms.

West et al. (1998) apply another special case of this flexible formulation, with autoregressive components, to an analysis of their complete hospital quality monitor data for the years 1988-1997. Related posterior computations are reviewed by Leonard and Hsu (1999,

Chapter 6). Harrison et al. (1977) apply a stochastic growth model for multinomial probabilities to a practical multiple time series analysis, for proportionate world sales of fibers, but without logit transformations. Autoregressive processes for multinomial logits were proposed by Leonard (1973). Hsu and Leonard (1997) assume a continuous time Gaussian process for binomial logits in a semi-parametric regression context. This formulation may also be used to model a possibly multiple time series, thus facilitating interpolations between the time points.

5. PRACTICAL PRIOR CHOICES

The broad prior assumptions at Stage 4 of our probability model permit a wide spectrum of representation of prior beliefs, depending upon the information or views possessed by the statistician analyzing the data. However, in some practical situations, information external to the current data set may be sparse. In these circumstances, pragmatic choices should be made. For example, the values $d_0 = d_1 = 1$ lead to a uniform distribution for η on the unit interval. We will also assume that, for some specified n_0, the parameter

$$\rho_0 = n_0/(n_0 + \gamma) \tag{5.1}$$

is a priori uniformly distributed over the equally spaced grid of points $i/(k+1)$ for $i = 1, 2, \ldots, k$. Then the Stage 4 distribution for γ assigns equal prior probabilities $\pi_i = 1/k$ to the unequally spaced points

$$g_i = n_0(k - i + 1)/i \quad (i = 1, 2, \ldots, k) \ . \tag{5.2}$$

Since $E(\rho_0) = 1/2$, n_0 provides a prior estimate for γ, which is more sensible than the prior mean of γ. As k gets large, the distribution of ρ_0 approaches a continuous uniform distribution on the unit interval. In this limiting case γ possesses a Cauchy-tail prior density $\pi(\gamma) = n_0/(n_0 + \gamma)^2$, for $0 < \gamma < \infty$. No prior mean for γ exists in the limiting case owing to the extremely thick right tail of the prior distribution. The Cauchy-tail density contrasts with the log-Cauchy prior density assumed by Crook and Good (1982) for a multinomial smoothing parameter. In the current situation, the limiting conditional posterior density of γ given the ξ_i is

$$\pi(\gamma|\mathbf{y}, \boldsymbol{\xi}) \propto \pi(\gamma) \prod_{i=1}^{m} l_i^*(\xi_i, \gamma) \ , \tag{5.3}$$

for $0 < \gamma < \infty$, where the contributions l_i^* to the product on the right hand side are defined in (3.3). Each ξ_i^* converges to unity as $\gamma \to \infty$, for any fixed ξ_i and y_i. Therefore the upper right tail of (5.3) invariably behaves like the upper right tail of $\pi(\gamma)$, for large values of γ.

Quite interestingly, if an improperly unfinitely uniform distribution with density $\pi(\gamma) \propto 1$, for $0 < \gamma < \infty$, is instead assumed for γ, then the density in (5.3) will never represent a proper distribution, thus invalidating the entire analysis. The Cauchy-tail prior density more appropriately controls the right tail of (5.3). This specification nevertheless represents quite sparse prior information regarding γ.

The parameter ρ_0 plays a somewhat similar role to the ρ_i satisfying (3.5) and (3.6), and can be interpreted as a shrinkage proportion relating to a hypothetical binomial experiment with sample size n_0. Under a beta prior distribution for θ_i with sample size γ and mean ξ_i, the posterior mean of θ_i, given only the hypothetical sample proportion p_0, is the weighted average compromise $\theta_i^o = \rho_0 p_0 + (1 - \rho_0)\xi_i$. A uniform distribution for γ rather than ρ_0, on an equally spaced grid, is much less appealing. This will become infinitely uniform as the width of the entire grid becomes large.

The choice of k should be based partly on considerations of computational simplicity. In practice, our prior assumptions for γ will however typically be justifiable only if the posterior inferences are insensitive to the choices of k and the prior estimate n_0. Convenient ways of summarizing the sensitivity analysis are indicated in section 8. Reference will be made to a baseline value n^* for n_0, equal to the value of γ for which the average shrinkage proportion $\bar{\rho}$ in (3.6) is equal to 1/2. In pragmatic terms, n^* can be regarded as the value of γ for which, given the observed sample sizes, we judge the monotonicity hypothesis and a general alternative hypothesis to possess equal weight. When all the n_i are equal, n^* is equal to their common value. More generally n^* describes a robust center of location for the n_i.

With η, γ, and λ a priori independent, it is similarly assumed that, for some specified λ_0, the parameter

$$\zeta_0 = \lambda_0/(\lambda_0 + \lambda) \tag{5.4}$$

is uniformly distributed over the equally spaced grid of points $i/(l+1)$, for $i = 1, 2, \ldots, l$. The corresponding distribution for λ assigns equal prior probabilities $\delta_i = i/(l+1)$ to the unequally spaced points

$$h_i = \lambda_0(l - i + 1)/i \quad (i = 1, 2, \ldots, l) \ , \tag{5.5}$$

yielding the Cauchy-tail prior density $\pi(\lambda) = \lambda_0/(\lambda_0 + \lambda)^2$, for $0 < \lambda < \infty$, in the limiting

case, or l gets large. A sensitivity analysis with respective to the choices of l and the prior estimate λ_0 of λ should also be performed. As an alternative specification, the shrinkage proportion ζ in (4.5) could be taken to be uniformly distributed over the same grid. In this case γ and λ would not be independent.

When γ and λ are independent it may be reasonable to replace γ in (4.5) by its prior estimate n_0 before taking ζ to be uniformly distributed. This is the same as taking ζ_0 in (5.4) to be uniformly distributed, with the choice $\lambda_0 = n_0 + 1$ for the prior estimate of λ. Our prior estimate for the shrinkage proportion ζ, which controls the weighted average compromise (4.3), is then equal to the neutral value of 1/2. The specification $\lambda_0 = n_0 + 1$ should not therefore unduly bias our investigation of the monotonicity hypothesis, and is consequently recommended as a baseline choice. The initial baseline selections $n_0 = n^*$ and $\lambda_0 = n^* + 1$, when followed by a careful sensitivity analysis, promise a reasonably fair evaluation of the information regarding possible monotonicity contained in the current data.

Let $\tilde{\rho}^*$ and $\tilde{\zeta}^*$ denote the posterior means of the bounded parameters $\tilde{\rho} = n^*/(n^* + \gamma)$ and $\tilde{\zeta} = (n^* + 1)/(n^* + \lambda + 1)$ under the preceding prior assumptions, where the prior parameters n_0 and λ_0 may differ from the values n^* and $n^* + 1$. The posterior means of the unbounded parameters γ and λ invariably become arbitrarily large as k and l get large. We therefore recommend estimating γ and λ in the posterior assessment by the inverse transformations

$$\gamma^* = n^*(1 - \tilde{\rho}^*)/\tilde{\rho}^* \quad , \tag{5.6}$$

and

$$\lambda^* = (n^* + 1)(1 - \tilde{\zeta}^*)/\tilde{\zeta}^* \quad . \tag{5.7}$$

Unconditional posterior inferences for the θ_i and ξ_i promise to be reasonably insensitive to the choices of k and l, since their posterior distributions, given γ and λ, depend only upon bounded functions of γ and λ.

6. A TIME SERIES ANALYSIS FOR A SAFARI CAT

We analyze the data for cat 40665, firstly under our Stage 1 binomial sampling assumptions. The $\tilde{\theta}_i^*$ in the fifth column of Table 2 describe posterior means for the proportions θ_i of domestic type cells in the full progenitor pools at time t_i (see second column) as discussed in section 2.2, and for the data introduced in Table 1, with $m = 18$. The analysis in the present section does not accommodate the unequally spaced nature of the t_i, and will

therefore be qualified in section 7. By reversing the order of the data our computer program may be used to investigate the possibility of monotonic decreasing, rather than monotonic increasing, population proportions.

(Table 2 is about here)

The posterior analysis is based upon the prior formulations of sections 3 and 5, with the choices $k = l = 24$. The grids for the parameters ρ_0 in (5.1) and ζ_0 in (5.4) therefore each split the unit interval into 25 intervals of equal width 0.04. However, almost identical numerical results, to three decimal places, were obtained for all entries in the third to sixth columns of Table 2, when instead $k = l = 49$, and when $k = l = 99$. All of these entries, when accurately simulated, will approximate limiting quantities as k and l get large. However, the sensitivity analysis conducted in the present section suggests that the choices $k = l = 24$ will suffice, unless greater accuracy is required for particular posterior quantities, when compared with the precision of the further results discussed below.

We initially assume the values $n_0 = n^* = 73.65$ and $\lambda_0 = n^* + 1 = 74.65$ as prior estimates for γ and λ. The baseline value n^* was obtained by setting $\bar{\rho}$ in (3.6) equal to 0.5. and then solving for γ using a standard Newton-Raphson procedure, with $\bar{n} = 77.17$ as starting value. While the baseline values would seldom reflect prior beliefs, we will show in section 8 that the posterior analysis is reasonably insensitive to other choices of n_0 and λ_0, which might be elicited from subjective prior beliefs or opinions.

The posterior estimates for γ and λ, satisfying (5.6) and (5.7), are $\gamma^* = 46.91$ and $\lambda^* = 15.92$. These values compare with $\gamma^* = 46.08$ and $\lambda^* = 15.78$ when instead $k = l = 49$, and with $\gamma^* = 46.98$ and $\lambda^* = 15.86$ when instead $k = l = 99$. When $k = l = 24$, the posterior means of the average shrinkage proportion $\bar{\rho}$ in (3.6), the shrinkage proportion ζ in (4.5), and the common location parameter η for the ξ_i are respectively 0.610, 0.733, and 0.528, with associated posterior standard deviations 0.130, 0.158, and 0.038. The preceding six numerical values contrast with the values 0.608, 0.735, 0.528, 0.133, 0.156, and 0.038 when instead $k = l = 49$, and with the values 0.609, 0.733, 0.529, 0.133, 0.158, and 0.038 when instead $k = l = 99$.

The posterior means $\tilde{\theta}_i^*$ of the θ_i in Table 2 smooth the p_i substantial proportions of the distances towards the corresponding, strictly decreasing, posterior means $\tilde{\xi}_i^*$ of the ξ_i. For example, $\tilde{\theta}_{12}^* = 0.473$ shrinks $p_{12} = 0.466$ about 41% of the distance towards $\tilde{\xi}_{12}^* = 0.483$. Therefore, while the $\tilde{\theta}_i^*$ are not monotonic decreasing they are substantially smoothed in the

light of a monotonic decreasing prior hypothesis. The posterior standard deviations of the θ_i are reported in the sixth column of Table 2. With the exception of std(θ_6) they are less than the corresponding s_i. The value $p_6 = 0.789$ is the observed proportion most in conflict with the monotonicity hypothesis.

(Table 3 is about here)

The entries π_i^* to the third column of Table 3 describe the posterior probabilities for γ corresponding to the values for γ in the second column. The entries δ_i^* to the last column describe the posterior probabilities for λ corresponding to the values for λ in the fifth column. The marginal posterior distributions of γ and λ are both quite informative, with interior modes and steadily decreasing right and left tails, despite the diffuse properties of the prior distribution.

The entries to the fourth column of Table 3 denotes the values for $\bar{\rho}$ in (3.6) matching the values for γ in the second column. The π_i^* hence also define the marginal posterior distribution of $\bar{\rho}$. Under binomial assumptions, we recommend partly basing an overall appraisal of the monotonicity hypothesis upon an applied evaluation of this marginal distribution, a process which should where possible refer to experience with previous data sets. A concentration of this distribution towards zero provides evidence in favor of the monotonicity hypothesis. A concentration toward unity provides evidence against the monotonicity hypothesis. The posterior probability

$$\tau = p(\bar{\rho} \leq 0.5|\mathbf{y}) = p(\gamma \geq n^*|\mathbf{y}) \tag{6.1}$$

may be usefully considered. Remember from (3.5) and (3.6) that, given γ and the ξ_i, $\bar{\rho} = 1/2$ provides a neutral average value for the shrinkage proportions ρ_i, which measure the way the θ_i^* compromise between the p_i and the ξ_i. In our example $\tau = 0.194$. It instead $k = l = 99$, then $\tau = 0.204$. The qualified analysis of section 7 suggests a reduction to $\tau = 0.136$. These values together with a general appraisal of the posterior distribution, draw us to the conclusion that, even under strict binomial sampling assumptions with all their practical implications, there is insufficient evidence in the data to entirely refute a monotonic decreasing hypothesis..

It is also possible to draw posterior inferences regarding the monotonic decreasing random population proportions ξ_i, under our beta-binomial sampling assumptions The posterior means $\tilde{\xi}_i^*$ in Table 2 smooth the corresponding unordered sample proportions p_i quite substantially. The posterior standard deviations of the ξ_i are reported in the eighth column. In

the ninth column we however report the conceptually difference quantities

$$s_i^* = (D_i^*)^{\frac{1}{2}}\{\tilde{\xi}_i^*(1-\tilde{\xi}_i^*)/n_i\}^{\frac{1}{2}} \tag{6.2}$$

for $i = 1, 2, \ldots, m$, where $D_i^* = (n_i + \gamma^*)/(1+\gamma^*)$ with $\gamma^* = 46.91$. The s_i^* provide estimated standard errors for the sample proportions p_i. They are appropriate under the conditional independent beta-binomial sampling model obtained by combining just the first two stages of our probability model. The point estimates $\gamma^* = 46.91$ and $\xi_1^* = 0.753, \xi_2^* = 0.691, \ldots, \xi_{18}^* = 0.283$ are imputed for the model parameters. Owing to over-dispersion the values for the s_i^* substantially inflate the s_i, which are only appropriate under binomial assumptions.

The entries in the last column of Table 2 describe the normalized residuals

$$r_i = (p_i - \tilde{\xi}_i^*)/s_i^* \quad , \tag{6.3}$$

for $i = 1, 2, \ldots, m$. The r_i may be used to judge the plausibility of our model specification of monotonic decreasing ξ_i. With the exception of $r_6 = 2.109$ all of the residuals are reassuringly small. There is no particular pattern in the r_i which might refute the monotonicity specification for the ξ_i. An intuitive overall evaluation of our monotonicity specification may be made by reference to the average squared normalized residual

$$W = \sum_{i=1}^{m} r_i^2/m \quad . \tag{6.4}$$

In the current example, $W = 0.873$. If instead $k = l = 49$ or $k = l = 99$ then $W = 0.874$. The qualified analysis of section 7 suggests that $W = 0.918$. By essential reference also to our preceding residual analysis, and to the implications, discussed in section 4.1, in the context of isotonic regression, of the flattening property described there, we are drawn to a key conclusion. The current data appear to be largely consistent with the monotonicity specification of the form $\xi_1 \geq \xi_2 \geq \cdots \geq \xi_{18}$, under our beta-binomial sampling assumptions with a common parameter γ. The posterior means and standard deviations of the ξ_i should also be considered, together with the experimental nature of the sampling methods employed by Abkowitz et al. (1988), and the related possibility of deviations from our beta-binomial model. The underlying population proportions ξ_i may well be noticeably strictly decreasing. Further overall conclusions are stated towards the end of section 7.

7. AN INTERPOLATION PROCEDURE

The analysis of section 6 is now qualified by taking into account the unequally spaced nature of the time points. An interpolation device is employed. For the posterior analysis summarized in Table 2, the times t_i, while not equally spaced, comprise a subset of an equally spaced lattice within boundaries $t_1 = 10$ and $t_{18} = 60$. In the second column of Table 4, the times t_i are instead equally spaced, for $i = 1, 2, \ldots, 51$, with $t_1 = 10$ and $t_{51} = 60$. They include the sampling times in Table 2, together with 33 interpolated points.

(Table 4 is about here)

The positive values for the y_i and n_i in the third and fourth columns of Table 4 comprise the data from Table 1 for the original time points. The values $y_i = 0$ and $n_i = 0$ are imputed at all interpolated time points. Our general formulation and methodology may be applied to the $m = 51$ situation. The conditional posterior distribution of θ_i, given ξ_i and γ, is beta with mean ξ_i and sample size γ, the prior specification, at all interpolated time points. As $n_i p_i = y_i$, the conditional posterior mean in (3.4) reduces to ξ_i whenever $y_i = n_i = 0$. Consequently, at our interpolated time points, the unconditional posterior mean of θ_i always equals the unconditional posterior mean of ξ_i, and the unconditional posterior variance of θ_i always exceeds the unconditional posterior variance of ξ_i.

With $k = l = 24$, we initially assume the prior estimates $n_0 = n^* = 73.65$ and $\lambda_0 = n^* + 1 = 74.65$ for γ and λ. These yield the posterior estimates $\gamma^* = 42.72$ and $\lambda^* = 18.88$. The posterior means of $\bar{\rho}$, ξ, and η are respectively 0.632, 0.684, and 0.500, where $\bar{\rho}$ is slightly redefined below. The corresponding posterior standard deviations are 0.117, 0.158, and 0.029.

The posterior means $\tilde{\xi}_i^*$ for the ξ_i in the penultimate column of Table 4 are strictly decreasing. For the original time points, the $\tilde{\xi}_i^*$ only slightly differ from the values in Table 2. Quite appealing values are reported at the interpolated time points. For example, the three decreasing values $\tilde{\xi}_{25} = 0.506$, $\tilde{\xi}_{26} = 0.499$, and $\tilde{\xi}_{27} = 0.493$ now interpolate the values $\tilde{\xi}_{24} = 0.512$ and $\tilde{\xi}_{28} = 0.486$ at the time points $t_{24} = 33$ and $t_{28} = 37$, for which we previously recorded the estimates $\tilde{\xi}_{11} = 0.504$ and $\tilde{\xi}_{12} = 0.483$.

At the original time points, the posterior means $\tilde{\theta}_i^*$ for the θ_i, as reported in the seventh column of Table 4, only slightly differ from the values recorded in Table 2. As theoretically required, the $\tilde{\theta}_i^*$ for the interpolated time points indeed equal the corresponding imputed $\tilde{\xi}_i$. The posterior standard deviations of the θ_i however substantially inflate those of the ξ_i at these time points, as reported in the eighth and tenth columns of Table 4.

When providing overall measures of discrepancies from monotonicity, we slightly redefine $\bar{\rho}$ in (3.6) and W in (6.4). Just average the ρ_i in (3.5) and W in (6.4) over those $i = 1, 2, \ldots, m$ for which $n_i > 0$. With these provisos, $W = 0.918$, and τ in (6.1) equals 0.136. A residual analysis, not fully reported here, provides normalized residuals at all the original time points, and very similar conclusions to the analysis recorded in Table 2. For example, $r_{12} = 2.198$. Overall, the key conclusions, reported in section 6 are further substantiated. When comparing the results in sections 6 and 7, we also conclude that not too much information is lost by ignoring the unequally spaced nature of the time points. This conclusion is also of relevance to isotonic regression, and further motivates our method of analysis in sections 2.1, 4.3 and 9.

The interpolation device may also be used to omit observations corresponding to large residuals. For example, when $y_{12} = 90$ and $n_{12} = 114$ are replaced by $y_{12} = n_{12} = 0$, W increases to 0.984, while τ increases substantially to 0.496. Under strict binomial sampling assumptions, we would conclude that the monotonicity hypothesis is much more consistant with the data, when considered at all eighteen of the original sampling times, but with the exception of t_{12} (previously t_6) = 21. This conclusion compares with the initial sampling assumptions made by Newton et al. However, when seeking to justify our monotonicity hypothesis under extra-binomial sampling assumptions, we would include the data for all eighteen original sampling times. For the modified analysis, $n_0 = n^* = 71.77$, $\lambda_0 = n^* + 1 = 72.77$ and $\bar{\rho}$, ζ, and η possess posterior means 0.486, 0.744, and 0.487, with respective standard deviations 0.167, 0.150, and 0.027.

8. SENSITIVITY ANALYSIS

The entries in Table 5 summarize the sensitivity of the posterior conclusions of section 6 to the choices of the prior estimates n_0 and λ_0 for γ and λ, when $k = l = 25$. Just 20,000 simulations were performed after burn-in, for each choice of n_0 and λ_0, but with the same random numbers for each new choice of n_0 and λ_0, to preclude differences due to simulation error. The more precisely calculated posterior conclusions, subject to the baseline choices $n_0 = n^* = 73.65$ and $\lambda_0 = n^* + 1 = 74.65$, are recorded in the last row.

(Table 5 is about here)

The bounded functions $\bar{\rho}$ and ζ usefully reparameterize γ and λ, and provide overall summaries of the posterior smoothing of the θ_i and ξ_i. Their posterior means and standard

deviations are reported in the second to fifth columns of Table 5. The differences between these values, across the ranges of values of n_0 and λ_0 considered, are reasonably small. The posterior means and standard deviations of the location parameter η are not reported here, since they are closely approximated by 0.528 and 0.038 for all these choices of n_0 and λ_0.

The first seven rows of Table 5 refer to the sensitivity of the posterior analysis when $\lambda_0 = n_0 + 1$. Noting that $n_0 = 70$ is close to the baseline value $n^* = 73.65$, we see that the entries in the second to fifth columns are reasonably insensitive to choices of n_0 between 10 and 130. Consequently, if indeed $\lambda_0 = n_0 + 1$, the conclusions of section 6 should appeal to subjective Bayesians, unless they possess substantial prior information for or against the monotonicity hypothesis for the θ_i.

The eighth to thirteenth rows instead fix $n_0 = 70$ and relax the assumption $\lambda_0 = n_0+1$ by varying λ_0. All entries in the second to seventh columns are remarkably insensitive to choices of λ_0 between 10 and 130. As $n^* = 73.65$ would yield similar results, this further validates the conclusions of section 6. The fourteenth to fifteenth rows refer to more extremely contrasting values of n_0 and λ_0. While the differences for the entries in the second to fifth columns are now substantial, they are not overwhelming. The value $n_0 = 10$ expresses, in the current context, a relatively strong prior belief that the monotonicity hypothesis for the θ_i is untrue.

The entries in the sixth and seventh columns report the diagnostic quantities τ and W. Unless $n_0 = 10$, all entries are reasonably insensitive to the choices of n_0 and λ_0 Very similar conclusions are available regarding the sensitivity of the posterior analysis of section 8, though the posterior mean and standard deviation of η were slightly more sensitive to changes to η_0 and λ_0. We in general recommend performing a preliminary sensitivity analysis, before proceeding to the main analysis, with a large number of simulations.

9. PERFORMANCE INDICATORS FOR QUALITY MONITORING

The conclusions described in section 2.1 for the data introduced there are now discussed further. The solid plot in Figure 1 describes the piecewise linear isotonic regression, defined in section 4.2, of the ξ_i, upon the 1992 raw proportions x_i. Smoothed performance indicators $\tilde{\xi}^*_1, \tilde{\xi}^*_2, \ldots, \tilde{\xi}^*_{159}$ for 1993, under conditionally independent beta-binomial assumptions, are thereby available. This ordering is consistent with the rank ordering of raw proportions for 1992. The posterior standard deviations of the ξ_i decrease from $\text{std}(\xi_1) = 0.032$ (with $n_1 = 350$ and $s_1 = 0.022$) to $\text{std}(\xi_{69}) = 0.10$ (with $n_{69} = 786$ and $s_{69} = 0.017$). They then increase from $\text{std}(\tilde{\xi}^*_{109}) = 0.010$ (with $n_{109} = 301$ and $s_{109} = 0.027$) to $\text{std}(\tilde{\xi}^*_{159}) = 0.031$

(with $n_{159} = 481$ and $s_{159} = 0.022$). They are however generally much smaller than the corresponding s_i.

After an initial sensitivity analysis, it was assumed that $k = 99$ and $l = 24$. The baseline values $n^* = 242.77$ and $n^* + 1 = 243.77$ are employed for γ_0 and η_0, and the posterior conclusions can again be shown to be reasonably insensitive to these assumptions. The posterior estimates for γ and λ are $\gamma^* = 25.99$ and $\lambda^* = 106.46$. As $\bar{\rho}$ has posterior mean 0.862 and standard deviation 0.013, with τ virtually equal to zero, there is negligible evidence to substantiate (1.1) under binomial sampling assumptions. As the shrinkage proportion ζ has posterior mean 0.214 and standard deviation 0.071, the $\tilde{\xi}_i^*$ are substantially smoothed towards a common value. The location parameter η possesses posterior mean 0.439 and standard deviation 0.010.

The average squared normalized residual is $W = 1.006$. A full residual analysis, though not reported here, can be roughly inferred from Figure 2. This indicates that the data are largely consistent with (3.1). In other words, the performance indicators for 1993 are largely consistent with the rank ordering for 1992 when sensible extra-binomial variation is permitted. The most discrepant r_i, for hospitals 39, 44, 66, 77, 153, 157, and 158, were respectively 2.51, 2.38, 2.84, 2.36, 2.79, -3.56, and 2.76, corresponding to the sample sizes 220, 20, 40, 1630, 176, 702, and 78. However, when the four hospitals 39, 77, 153, 157 were dropped from the analysis a larger value of $W = 1.037$ was obtained. Moreover, several further discrepant residuals appeared. It was therefore decided to include all original 159 hospitals in the analysis.

The two dotted plots in Figure 1 graph the $p_i - s_i^*$ and the $p_i + s_i^*$ where s_i^* in (6.2) is the estimated standard error of p_i under independent beta-binomial sampling assumptions. These estimated standard errors are quite large, ranging in magnitude from 0.092 to 0.237, though mainly in the region of 0.10. For a typical sample size of 250 our extra-binomial assumptions inflate the estimated standard errors by a factor of 3.20. The predictions of sample proportions for future years, with comparable sample sizes, are likely to be subject to greater random variability.

The solid graph in Figure 2 indicates that the performances for 1993 are also largely consistent with the rank ordering of the DRG predictions. The analysis assumed the same prior parameters as for Figure 1 and yielded $W = 1.005$, $\gamma^* = 24.38$, and $\lambda^* = 101.17$. The posterior means of $\bar{\rho}$, ζ, and η were 0.868, 0.209, and 0.443, with respective posterior standard

deviations 0.013, 0.059, and 0.010. There is a remarkable similarity with the corresponding posterior quantities underlying the analysis for Figure 1. This further emphasizes the close comparability of the predictive performances of the quite different rank orderings, based upon the 1992 raw indicators, and the DRG predictions for 1993.

The accuracy of prediction from this noisy data set is open to some improvement by reference to the binomial logit/normal random effects time series formulation employed by West et al. (1998). See also Aguilar et al. (1999). This general paradigm offers considerable scope for incorporating information from years previous to 1992, and combining information across the hospitals. For, say 1993, West et al. assume a simple linear regression for the binomial logits, upon the logits of the DRG predictions. Separate fixed effects regression parameters are estimated for each year. Random error terms, expressing assumed autoregressive time dependence and the representing the substantial residual variation in the data, are added to the regression functions. Any estimated standard errors of the sample proportions should refer to appropriate marginal distributions under random effects assumptions, since these can express the extra-binomial variability inherent in the data. West et al. demonstrate that the total lower level random effects variability is very large, thus again highlighting possible difficulties with prediction. They obtain very useful descriptive conclusions regarding the regression coefficients. More generally, the usefulness of performance indicators and quality monitoring, for predictive rather than descriptive purposes, is open to further discussion when the data are not objectively generated by random sampling schemes.

APPENDIX 1: A SIMPLE APPROXIMATION

Let $\theta|\xi \sim \text{Beta}\{\gamma\xi, \gamma(1-\xi)\}$, where $\xi \sim \text{Beta}(b_0, b_1)$, with $b_0 = \lambda\eta$ and $b_1 = \lambda(1-\eta)$. For fixed γ, λ, and η, we consider the approximation

$$\xi|\theta \sim \text{Beta}\{(\gamma+1)\theta + b_0, (\gamma+1)(1-\theta) + b_1\} \tag{1}$$

to the conditional distribution of ξ given θ. In Figure 3 we compare the corresponding approximate and exact densities, for the choices $\eta = 0.3$, $\gamma = 10$ and $\lambda = 11$, so that $b_0 = 3.3$ and $b_1 = 7.7$, and for six different values (0.05, 0.25, 0.40, 0.60, 0.75, and 0.95) of θ. The approximate (dotted) curves are close to the corresponding exact (solid) curves, unless θ is very different from λ. It is also possible to show that they substantially increase in accuracy as b_0, b_1 or γ increases. Some slight algebraic rearrangement of (1) justifies the approximation in (4.2) and a modest extension suggests the approximation in (4.7).

(Figure 3 is about here)

The approximation in (1) may be motivated by noting that, given ξ, $\tilde{y} = (\gamma+1)\theta$ possesses mean $\tilde{n}\xi$ and variance $\tilde{n}\xi(1-\xi)$ where $\tilde{n} = \gamma + 1$. By matching first two moments, we see that when $\tilde{n}$ is an integer, a specified value of $\tilde{y}$ provides similar information regarding ξ as if $\tilde{y}$ represented the realization of a BIN$(\xi, \tilde{n})$ variate. This indicates the plausibility of the discrete approximation, $(\gamma+1)\theta|\xi \sim$ BIN$(\xi, \tilde{n})$ to the continuous exact distribution. Subject to this approximation, the conjugate analysis for the binomial distribution, then tells that $\xi|\tilde{y} \sim$ Beta$\{b_0 + \tilde{y}, b_1 + \tilde{n} - \tilde{y}\}$, which is equivalent to (1). Our derivation is not however as convincing as the numerical comparisons. The result certainly needs to be inferred and subsequently numerically validated in situations when $\tilde{n}$ is not an integer.

APPENDIX 2: POSTERIOR COMPUTATIONS

We employ standard Metropolis algorithm/MCMC procedures based upon successive simulations from the following conditional distributions, which all refer to the joint distribution of the θ_i, ξ_i, γ, λ, and η, conditional on the observed data:
(D1) Given the ξ_i and γ, the θ_i are independent and beta distributed, with respective sample sizes $n_i + \gamma$ and means in (3.4). (When $n_i = 0$, θ_i possesses a beta distribution with sample size γ and mean ξ_i.)
(D2) Given the θ_i, γ, η, and λ, an approximate joint distribution for the ξ_i constrains the m independent distributions in (4.2) to the region (3.1).
(D3) The distribution of γ, given the ξ_i, but unconditional upon the θ_i, assigns probabilities π_1^*, π_2^*, ..., π_k^* to the points $g_1, g_2, \ldots, g_k$, where

$$\pi_i^* \propto \pi_i l^*(h_i|\boldsymbol{\xi}, \mathbf{y}) \quad , \tag{2}$$

for $i = 1, 2, \ldots, m$, with $\pi_1, \pi_2, \ldots, \pi_k$ denoting the corresponding prior probabilities, and

$$l^*(\gamma|\boldsymbol{\xi}, \mathbf{y}) = \prod_{k=1}^{m} l^*(\gamma|\xi_k, y_k) \quad , \tag{3}$$

where the contributions to the product on the right hand side of (3) are defined in (3.3). It is essential to refer to (2) rather than posterior probabilities for γ, given the ξ_i and θ_i, in order to avoid insurmountable instabilities in the posterior computations.

(D4) The distribution of λ, given η and the ξ_i, assigns probabilities δ_1^*, δ_2^*, ..., δ_l^* to the points $g_1, g_2, \ldots, g_l$, where

$$\delta_i^* \propto \delta_i \tilde{l}(\eta, g_i|\boldsymbol{\xi}) \quad , \tag{4}$$

for $i = 1, 2, \ldots, l$, with $\delta_1, \delta_2, \ldots, \delta_l$ denoting the corresponding prior probabilities, and $\tilde{l}(\eta, \lambda|\boldsymbol{\xi})$ defined in (4.10).

(D5) The distribution of η, given λ and the ξ_i, may be approximated by the beta distribution in (4.7).

The simulations from D2 can be made effectively exact. The constrained beta approximations can be handled by successive sampling from truncated beta distributions. When generating values for η, just simulate from the approximate distribution in (4.7). This conditional distribution can be highly concentrated, for large λ, about its mean in (4.8) and the corresponding exact density in (4.9) can be highly peaked around a slightly different location. Acceptance sampling for η can therefore lead to a high rejection rate. However, subject to our minor approximation, all posterior quantities of interest can be calculated in standard fashion.

About 200,000 successive simulations on all parameters are recommended for good practical accuracy, after an initial burn-in period of about 1,000 simulations. Good starting values in D1 are $\gamma = n^*$, our baseline prior estimate, and $\xi_i = p_i$ for $i = 1, 2, \ldots, m$. Increasing the numbers k and l of grid points too much will not necessarily provide completely exact representations of Bayesian inferences under a continuous prior distribution. The errors of our discrete approximation to a continuous posterior distribution will confound with the errors of simulation.

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Table 1: A Time Series for a Safari Cat

i	t_i	y_i	n_i	p_i	s_i	z_i
1	10	48	59	0.814	0.051	2.432
2	12	35	57	0.614	0.064	0.679
3	14	32	58	0.552	0.065	-1.137
4	16	43	66	0.652	0.059	0.672
5	18	35	59	0.593	0.064	-2.635
6	21	90	114	0.789	0.038	2.003
7	23	76	113	0.673	0.044	2.163
8	26	50	95	0.526	0.051	-0.681
9	29	40	69	0.580	0.059	-0.331
10	31	34	56	0.607	0.065	2.362
11	33	28	70	0.400	0.059	-0.746
12	37	27	58	0.466	0.065	-1.095
13	39	48	86	0.558	0.054	2.912
14	41	44	123	0.358	0.043	0.479
15	43	20	62	0.323	0.059	-1.786
16	51	27	56	0.482	0.067	3.178
17	57	30	126	0.238	0.038	-0.297
18	60	16	62	0.258	0.056	—

Table 2: Posterior and Residual Analysis

i	t_i	p_i	s_i	$\tilde{\theta}_i^*$	std(θ_i)	$\tilde{\xi}_i^*$	std(ξ_i)	s_i^*	r_i
1	10	0.814	0.051	0.789	0.046	0.753	0.057	0.083	0.722
2	12	0.614	0.064	0.649	0.052	0.691	0.043	0.090	-0.850
3	14	0.552	0.065	0.601	0.053	0.662	0.038	0.092	-1.200
4	16	0.652	0.059	0.649	0.047	0.644	0.036	0.090	0.086
5	18	0.593	0.064	0.609	0.050	0.627	0.035	0.094	-0.365
6	21	0.789	0.038	0.738	0.040	0.613	0.035	0.084	2.109
7	23	0.673	0.044	0.650	0.039	0.593	0.034	0.084	0.940
8	26	0.526	0.051	0.542	0.044	0.570	0.033	0.087	-0.496
9	29	0.580	0.059	0.568	0.048	0.550	0.032	0.093	0.321
10	31	0.607	0.065	0.572	0.052	0.529	0.033	0.098	0.800
11	33	0.400	0.059	0.441	0.049	0.504	0.033	0.093	-1.111
12	37	0.466	0.065	0.473	0.051	0.483	0.034	0.097	-0.185
13	39	0.558	0.054	0.524	0.047	0.463	0.035	0.090	1.064
14	41	0.358	0.043	0.378	0.039	0.433	0.038	0.084	-0.890
15	43	0.323	0.059	0.357	0.049	0.406	0.041	0.094	-0.888
16	51	0.482	0.067	0.435	0.055	0.380	0.043	0.095	1.071
17	57	0.238	0.038	0.262	0.036	0.331	0.051	0.080	-1.164
18	60	0.258	0.056	0.267	0.048	0.283	0.058	0.086	-0.286

Table 3: Posterior Probabilities

i	$\gamma = g_i$	π_i^*	$\bar{\rho}$	$\lambda = h_i$	δ_i^*
1	3.07	0.000	0.959	3.11	0.004
2	6.40	0.001	0.918	6.49	0.112
3	10.04	0.006	0.877	10.18	0.259
4	14.03	0.024	0.836	14.22	0.249
5	18.41	0.052	0.796	18.66	0.165
6	23.26	0.083	0.756	23.57	0.093
7	28.64	0.109	0.717	29.03	0.050
8	34.66	0.122	0.677	35.13	0.028
9	41.43	0.123	0.637	41.99	0.016
10	49.10	0.113	0.598	49.77	0.009
11	57.87	0.096	0.559	58.65	0.005
12	67.99	0.077	0.520	68.91	0.003
13	79.79	0.059	0.480	80.87	0.002
14	93.74	0.044	0.441	95.01	0.001
15	110.48	0.031	0.402	111.98	0.001
16	130.94	0.021	0.363	132.71	0.001
17	156.51	0.014	0.323	158.63	0.000
18	189.39	0.009	0.284	191.96	0.000
19	233.23	0.006	0.244	236.39	0.000
20	294.60	0.004	0.204	298.60	0.000
21	386.67	0.002	0.164	391.92	0.000
22	540.11	0.001	0.124	547.44	0.000
23	846.99	0.001	0.083	858.49	0.000
24	1767.62	0.000	0.042	1791.62	0.000

Table 4: Posterior Estimates and Imputations

i	t_i	y_i	n_i	p_i	s_i	$\tilde{\theta}_i^*$	std(θ_i)	$\tilde{\xi}_i^*$	std(ξ_i)
1	10	48	59	0.814	0.051	0.791	0.046	0.756	0.054
2	11	0	0	-	-	0.713	0.088	0.713	0.046
3	12	35	57	0.614	0.064	0.646	0.052	0.687	0.040
4	13	0	0	-	-	0.670	0.086	0.670	0.038
5	14	32	58	0.552	0.065	0.597	0.053	0.656	0.036
6	15	0	0	-	-	0.646	0.086	0.646	0.035
7	16	43	66	0.652	0.059	0.646	0.047	0.636	0.034
8	17	0	0	-	-	0.628	0.086	0.628	0.033
9	18	35	59	0.593	0.064	0.605	0.050	0.620	0.032
10	19	0	0	-	-	0.612	0.086	0.612	0.031
11	20	0	0	-	-	0.605	0.086	0.605	0.031
12	21	90	114	0.789	0.038	0.737	0.040	0.598	0.030
13	22	0	0	-	-	0.590	0.086	0.590	0.030
14	23	76	113	0.673	0.044	0.648	0.040	0.583	0.029
15	24	0	0	-	-	0.575	0.086	0.575	0.028
16	25	0	0	-	-	0.567	0.086	0.567	0.028
17	26	50	95	0.526	0.051	0.537	0.043	0.560	0.028
18	27	0	0	-	-	0.553	0.086	0.553	0.027
19	28	0	0	-	-	0.546	0.086	0.546	0.027
20	29	40	69	0.580	0.059	0.565	0.048	0.539	0.027
21	30	0	0	-	-	0.533	0.086	0.533	0.027
22	31	34	56	0.607	0.065	0.573	0.052	0.526	0.027
23	32	0	0	-	-	0.519	0.087	0.519	0.027
24	33	28	70	0.400	0.059	0.442	0.049	0.512	0.027
25	34	0	0	-	-	0.506	0.087	0.506	0.028
26	35	0	0	-	-	0.499	0.087	0.499	0.028
27	36	0	0	-	-	0.493	0.087	0.493	0.028
28	37	27	58	0.466	0.065	0.474	0.051	0.486	0.028
29	38	0	0	-	-	0.480	0.087	0.480	0.029
30	39	48	86	0.558	0.054	0.530	0.046	0.474	0.029

Table 4 (Continued)

i	t_i	y_i	n_i	p_i	s_i	$\tilde{\theta}_i^*$	std(θ_i)	$\tilde{\xi}_i^*$	std(ξ_i)
31	40	0	0	-	-	0.467	0.087	0.467	0.030
32	41	44	123	0.358	0.043	0.384	0.039	0.460	0.031
33	42	0	0	-	-	0.453	0.088	0.453	0.031
34	43	20	62	0.323	0.059	0.372	0.050	0.446	0.032
35	44	0	0	-	-	0.440	0.088	0.440	0.033
36	45	0	0	-	-	0.434	0.088	0.434	0.034
37	46	0	0	-	-	0.427	0.088	0.427	0.035
38	47	0	0	-	-	0.420	0.088	0.420	0.035
39	48	0	0	-	-	0.413	0.089	0.413	0.036
40	49	0	0	-	-	0.406	0.089	0.406	0.037
41	50	0	0	-	-	0.399	0.089	0.399	0.038
42	51	27	56	0.482	0.067	0.442	0.054	0.391	0.039
43	52	0	0	-	-	0.382	0.089	0.382	0.040
44	53	0	0	-	-	0.372	0.090	0.372	0.042
45	54	0	0	-	-	0.361	0.090	0.361	0.044
46	55	0	0	-	-	0.349	0.091	0.349	0.045
47	56	0	0	-	-	0.336	0.091	0.336	0.047
48	57	30	126	0.238	0.038	0.258	0.036	0.320	0.049
49	58	0	0	-	-	0.304	0.091	0.304	0.051
50	59	0	0	-	-	0.283	0.092	0.283	0.054
51	60	16	62	0.258	0.056	0.253	0.048	0.250	0.057

Table 5: Sensitivity Analysis

n_0, λ_0	E($\bar{\rho}$)	std($\bar{\rho}$)	E(ζ)	std(ζ)	τ	W
10, 11	0.658	0.118	0.725	0.144	0.054	0.760
30, 31	0.634	0.125	0.723	0.160	0.159	0.819
50, 51	0.623	0.126	0.725	0.157	0.189	0.845
70, 71	0.615	0.134	0.721	0.170	0.206	0.867
90, 91	0.605	0.135	0.733	0.160	0.187	0.883
110, 111	0.600	0.134	0.736	0.160	0.183	0.894
130, 131	0.592	0.138	0.742	0.160	0.201	0.908
70, 10	0.600	0.133	0.776	0.130	0.234	0.872
70, 30	0.608	0.132	0.747	0.145	0.218	0.867
70, 50	0.612	0.133	0.733	0.156	0.210	0.867
70, 90	0.613	0.132	0.729	0.158	0.208	0.867
70, 10	0.615	0.133	0.720	0.163	0.202	0.867
70, 30	0.617	0.132	0.719	0.167	0.201	0.864
10, 30	0.675	0.115	0.656	0.183	0.042	0.756
130, 10	0.576	0.141	0.792	0.127	0.229	0.916
n^*, n^*+1	0.610	0.130	0.733	0.158	0.194	0.873

Figure 1: Raw Performance Indicators for 1992 and 1993

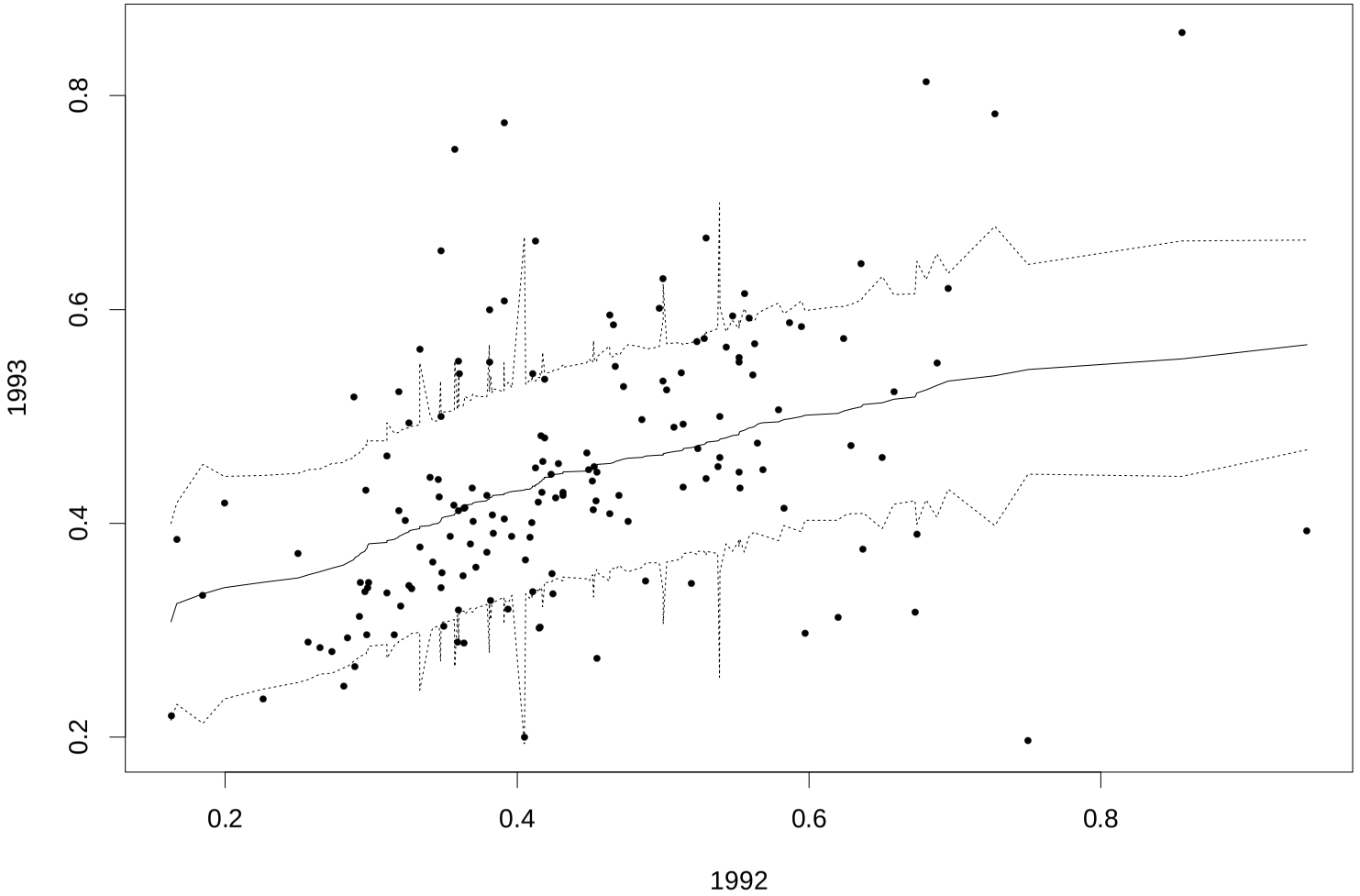

Figure 2: DRG Predictions and Observed Proportions for 1993

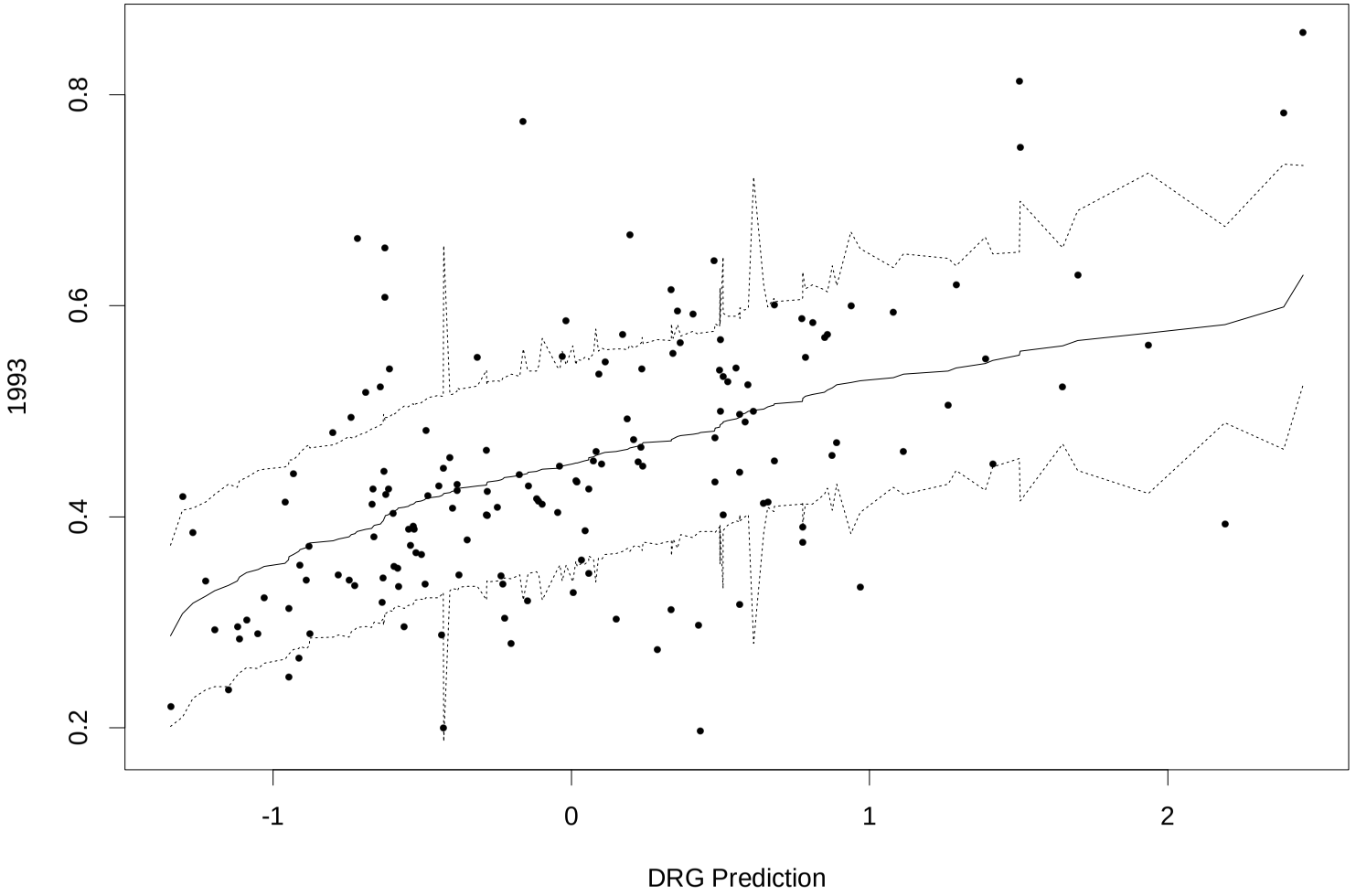

FIGURE 3: BETA APPROXIMATIONS