From: Sent: To:

Subject:

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RE what is the evidence base for MMR safety?

From: John Stone [mailto

Sent: 02 November 2018 15.02

To: Davies, Sally <sally.davies@dh.gsi.gov.uk>

Subject: What is the evidence base for MMR safety?

Dear Dame Sally,

I just wanted to point out the question which I have posed Drs Bedford and Elliman in on-line BMJ (see below). I don't think people who criticise vaccines are necessarily either malicious or incompetent. Many people quite reasonably want to know what the evidence base is for a medical intervention, and it cannot be simply that officials and experts know best.

With all good wishes,

John Stone

# Re: Measles: neither gone nor forgotten - but what is the evidence base for MMR safety?

Re: Measles: neither gone nor forgotten Helen Bedford, David Elliman. 362:doi 10.1136/bmj.k3976 I wonder if Helen Bedford and David Elliman [1] can assist? Daily opprobrium is heaped on things like "antivaccine sentiment" and "social media" for damaging the programme and putting children at risk, including recently the Chief Medical Officer, Dame Sally Davies, on the BBC [2]. But in fairness what is the evidence base for MMR safety (setting aside products like Pluserix and and Imravax which had to be withdrawn anyway [3])? Dame Sally says "It's a safe vaccination - we know that" [2] but she does not say how we know. Three times Cochrane told us that safety studies were "largely inadequate" [4]. We have this new found interest in publishing trial data [5], but in the case of MMR there does not seem to be any anyway. We also have serious questions being asked about the monitoring zeal of the licensing agencies into other vaccines [6,7,8].

So, if there are doubts surely it is not the public who are to blame, and blaming the public does not solve the issue. Where are the good studies and sound monitoring procedures that the public are entitled to, and how are properly informed citizens supposed to proceed in their absence?

- [1] Helen Bedford and David Elliman, 'Measles: neither gone nor forgotten, 25 September 2018, https://doi.org/10.1136/bmi.k3976
- [2] Philippa Roxby "Don't be taken in by anti-vaccine myths on social media", 1 November 2018, https://www.bbc.co.uk/news/health-45990874
- [3] http://apps.who.int/iris/bitstream/handle/10665/228497/WER6741 301-302.P...
- [4] John Stone, 'Response to David Oliver II (Risks of Vaccines)', 28 August
- 2018, https://www.bmj.com/content/362/bmj.k3596/rr-11

- [5] Nigel Hawkes, "Shocking" number of clinical trials are never reported, say MPs', BMJ 2018; 363 doi: <a href="https://doi.org/10.1136/bmj.k4582">https://doi.org/10.1136/bmj.k4582</a> (Published 30 October 2018)
- [6] Jørgensen L, Gøtzsche PC, Jefferson T. The Cochrane HPV vaccine review was incomplete and ignored important evidence of bias', BMJ Evid Based Med. 2018 Oct;23(5):165-168. doi: 10.1136/bmjebm-2018-111012. Epub 2018 Jul 27
- [7] Doshi P., 'Pandemrix vaccine: why was the public not told of early warning signs?', BMJ. 2018 Sep 20;362:k3948. doi: 10.1136/bmj.k3948
- [8] Jørgensen L, Doshi P, Gøtzsche P, Jefferson T., 'Challenges of independent assessment of potential harms of HPV vaccines.', BMJ. 2018 Sep 24;362:k3694. doi: 10.1136/bmj.k3694. No abstract available.

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39 Victoria Street Room 75 - 7th Floor London SW1H 0EU 020 7210 5151 sally.davies@dh.gsi.gov.uk www.gov.uk

12 November 2018

Dear Mr Stone

Thank you for your email of 2 November 2018.

Vaccine safety is extremely important and taken seriously, and the safety of MMR vaccines has remained under continual review. As with any vaccine, MMR vaccines can have side effects in some people, and these are listed in the product literature. The potential for side effects has to be balanced against the benefits of protection against what can be very serious and potentially life-threatening infections. When safety issues have been confirmed in the past these have been acted upon. Your e-mail refers to the action taken with Urabe mumps-containing vaccines, and another example includes the identification and precautions around the risk of immune thrombocytopenic purpura with MMR vaccines. Should emerging evidence confirm any new risks, I can assure you that appropriate action would be taken.

Specifically in relation to whether MMR vaccines may be a cause of autism, a substantial body of population-based research has found no evidence to suggest a causal association. This evidence (not just for MMR, but other types of vaccine) is available for review in the published medical literature, and was summarised in a meta-analysis in 2014 which is free to download

(https://www.sciencedirect.com/science/article/pii/S0264410X14006367?via%3Dihub).

In relation to vaccine safety monitoring more generally, I can assure you that systems are in place to keep safety under review. This includes continual review of suspected adverse reaction reports (such as those submitted through the Yellow Card Scheme), evaluation of GP and hospital-based health records linked to immunisations, review of worldwide data and close collaboration with international health authorities.

We know that confidence in the UK vaccine programme is at very high levels and the vast majority of parents choose to have their children protected by vaccination. Vaccines are one of the best public health interventions we have - saving lives and preventing millions of people from getting life-threatening diseases.

Yours sincerely

PROFESSOR DAME SALLY C DAVIES FRS FMedSci CHIEF MEDICAL OFFICER



Dame Sally Davies,

Chief Medical Officer to the British Government,

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21 November 2018

Dear Dame Sally,

Thank you for your letter of 12 November. I would point out that though you are quite right I am concerned about the rise in autism I specifically asked about the evidence base for MMR safety. That said it is reasonable to point out autism for a whole host of reasons is a much more serious problem in modern Britain (and elsewhere) than measles. When the DHSC last surveyed this problem in 2004-5 the overall ASD rate among school children was ~1% which was 5 times higher than the rate for those young people born between 1984-8 mostly before MMR was introduced, as reported in the equivalent 1999 survey. Since then your department has neglected to look at the issue (apart from a couple of failed adult autism surveys) as everything manifestly got worse, year on year [1,2].

As it is, a recent survey carried out by the Department of Health in Northern Ireland showed that the rate had risen from 1.2% in 2009 to 2.9%, while in Belfast it was as high as 4.7%. Moreover, 60% are educational Stage 5 [3], ie the most severe level of disability, so these are not cases that could previously have been missed because somehow subliminal. Educational data from across the nation and reports of collapse in educational services in the media testify that Northern Ireland is not an isolated case, but just better documented [4].

Regarding the meta-review by Taylor Vaccines are not associated with autism [5] which you cited I note that there are just six MMR related studies included all of which have major problems. Three of the studies show apparent protective effect of MMR vaccines against autism (Madsen 8% [6], Smeeth 14% or 22% [7] and Mrozek-Budzyn 83%!!! [8]) which suggests bias. Of the Madsen paper Cochrane 2005 warned [9]:

"The follow up of diagnostic records ends one year (31 Dec 1999) after the last day of admission to the cohort. Because of the length of time from birth to diagnosis, it becomes increasingly unlikely that those born later in the cohort could have a diagnosis"

It remains troubling that as with a number of studies from this Danish group the co-ordinator on behalf of US Centers for Diseases Control, Poul Thorsen, is wanted for financial fraud from the CDC, though not extradited to the US now after nearly 8 years [10].

Of the De Stefano paper Cochrane commented [9]:

"The conclusion, however, implied bias in the enrollment of cases which may not be representative of the rest of the autistic population of the city of Atlanta, USA where the study was set."

And indeed in 2014 the paper was repudiated by one of the leading authors, William Thompson [11]:

"I regret that my coauthors and I omitted statistically significant information in our 2004 article published in the journal Pediatrics. The omitted data suggested that African American males who received the MMR vaccine before age 36 months were at increased risk for autism. Decisions were made regarding which findings to report after the data were collected, and I believe that the final study protocol was not followed."

The study by Smeeth [7] is compromised by its patchy data source, the General Practice Research Database where the autism rate represented is perhaps only one tenth of cases diagnosed [12]. Cochrane commented [9]:

"In the GPRD - based studies (Black 2003; Smeeth 2004) the precise nature of controlled unexposed to MMR and their generalisability was impossible to determine..."

It remains problematic whether the unvaccinated in this study we genuinely unvaccinated.

Of the Uchiyama study [13] Cochrane commented [14]:

"The cohort study of Uchiyama 2007 was potentially affected by a different type of bias, considering that the participants were from a private clinic and that definitions of applied Autistic Spectrum Disorders (ASD) diagnosis and of methods used for ASD regression ascertainment were not clearly reported."

And the Uno study [15] will suffer from similar issues since the cases came from the same clinic. Moreover, in both instances the studies were far too small (904 persons and 413) to necessarily provide any clear result even if they had been better controlled.

Nor can the Taylor meta-analysis [5] cover up the entire absence of pre-marketing studies. In 1988-9 when the British government was persuaded to introduce Pluserix, MMR2 and Imravax there were no safety studies at all, and successive governments have been forced into the defence of a policy which they had embarked on without safety evidence.

As to the robustness of the yellow card reporting system I note the recent correspondence in the columns of BMJ On-Line regarding monitoring of Pandemrix vaccine from Wendy E Stephen and Clifford G Miller [16], which has serious implications for how the MHRA monitor all products. The MHRA has, of course, the ultimate conflict of being entirely funded by the manufacturers. It may be mentioned that in 1992 the Pluserix and Imravax vaccines were withdrawn not apparently by the British Government concerned about patient safety but by the manufacturers catching the government on the hop [17].

We are confronting a catastrophic situation among our young people with chronic illness replacing infectious illness as the main issue and cost to the state, and laying the emphasis on infectious

diseases (with endless hate campaigns in the media against critics labelled "anti-vaxxers") is a distraction, and a distortion of policy. It would be unfortunate if ministers were being advised about the safety of the programme on such a threadbare and inadequate basis. Re-examining the policy is both essential and urgent.

- [1] John Stone, 'Response to David Oliver I (The Indisputable Rise in Autism)', BMJ Rapid Responses 28 August 2018, <a href="https://www.bmi.com/content/362/bmj.k3596/rr-12">https://www.bmi.com/content/362/bmj.k3596/rr-12</a>
- [2] John Stone, 'What about autism?' BMJ Rapid Responses, 21 August 2018, https://www.bmj.com/content/362/bmj.k3596/rr-0
- [3] Information Analysis Directorate 'The Prevalence of Autism (including Asperger Syndrome) in School Age Children in Northern Ireland 2018', published 10 May 2018, <a href="https://www.health-ni.gov.uk/sites/default/files/publications/health/asd-children-ni-2018.pdf">https://www.health-ni.gov.uk/sites/default/files/publications/health/asd-children-ni-2018.pdf</a>
- [4] Responses to Viner RM, 'NHS must prioritise health of children and young people', <a href="https://www.bmj.com/content/360/bmj.k1116/rapid-responses">https://www.bmj.com/content/360/bmj.k1116/rapid-responses</a>
- [5] Luke E Taylor et al, 'Vaccines are not associated with autism: An evidence-based meta-analysis of case-control and cohort studies', Vaccine 2014, <a href="https://autismoevaccini.files.wordpress.com/2014/05/vaccines-are-not-associated-with-autism.pdf">https://autismoevaccini.files.wordpress.com/2014/05/vaccines-are-not-associated-with-autism.pdf</a>
- [6] Madsen et al, 'A Population-Based Study of Measles, Mumps, and Rubella Vaccination and Autism', NEMJ 2002, <a href="https://www.nejm.org/doi/full/10.1056/NEJMoa021134">https://www.nejm.org/doi/full/10.1056/NEJMoa021134</a>
- [7] Smeeth et al, 'MMR vaccination and pervasive developmental disorders: a case-control study.' Lance 2004, <a href="https://www.ncbi.nlm.nih.gov/pubmed/15364187">https://www.ncbi.nlm.nih.gov/pubmed/15364187</a>
- [8] Mrozek-Budzyn et al, 'Lack of association between measles-mumps-rubella vaccination and autism in children: a case-control study.' Pediatric Infectious Diseases Journal 2010, <a href="https://www.ncbi.nlm.nih.gov/pubmed/19952979">https://www.ncbi.nlm.nih.gov/pubmed/19952979</a>
- [9] Demicheli et al, 'Vaccines for measles, mumps and rubella in children.', Cochrane Database Syst Rev. 2005 Oct 19;(4):CD004407.
- [10] Office of Inspector General, US Department of Health and Human Services, Fugitive Profiles, <a href="https://oig.hhs.gov/fraud/fugitives/profiles.asp">https://oig.hhs.gov/fraud/fugitives/profiles.asp</a>

[11]

 $\frac{https://legislature.vermont.gov/assets/Documents/2016/WorkGroups/House%20Health%20Care/Bills/H.98/Witness%20Testimony/H.98~Jennifer%20Stella~William%20Thompson%20Statement~5-6-2015.pdf$ 

- [12] John Stone, 'An old story: the GPRD does not provide credible autism data' 11 February 2014 <a href="https://bmjopen.bmj.com/content/3/10/e003219.responses">https://bmjopen.bmj.com/content/3/10/e003219.responses</a>
- [13] Uchiyama et al, 'MMR-vaccine and regression in autism spectrum disorders: negative results presented from Japan.' J Autism Dev Disord. 2007 Feb;37(2):210-7.
- [14] Demicheli et al, 'Vaccines for measles, mumps and rubella in children.', Cochrane Systematic Review Intervention Version published: 15 February 2012, https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004407.pub3/full

[15] Uno et al, 'The combined measles, mumps, and rubella vaccines and the total number of vaccines are not associated with development of autism spectrum disorder: the first case-control study in Asia', Vaccine. 2012 Jun 13;30(28):4292-8. doi: 10.1016/j.vaccine.2012.01.093. Epub 2012 Apr 20.

[16] Responses to Godlee, 'A tale of two vaccines' BMJ 2018, https://www.bmj.com/content/363/bmj.k4152/rapid-responses

[17] Report, BMJ 26 September 1992, https://www.bmj.com/content/305/6856/777

Yours sincerely,

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21 November 2018

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#### CORRECTED

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[17] Report, BMJ 26 September 1992, https://www.bmi.com/content/305/6856/777

Yours sincerely,

John Stone

From the Chief Medical Officer Professor Dame Sally Davies FRS FMedSci





39 Victoria Street Room 75 - 7th Floor London SW1H 0EU 020 7210 5151 sally.davies@dh.qsi.gov.uk www.qov.uk

20 December 2018

Dear Mr Stone

Thank you for your further letter of 21 November regarding MMR vaccine safety.

The Autism Act 2009 places a duty on the Secretary of State for Health and Social Care to publish a strategy for meeting the needs of autistic adults in England, and to review it periodically. England's first Adult Autism Strategy 'Fulfilling and rewarding lives', was published in 2010 and in April 2014, the Strategy was updated with the publication of 'Think Autism', supported by revised Statutory Guidance in March 2015. You may be interested to know that on 5 December 2018, the Department of Health and Social Care (DHSC) announced that it would be launching a comprehensive review of 'Think Autism' to ensure it remains fit for purpose. The DHSC want an autism strategy that works for all autistic people, and that is why, working very closely with the Department for Education, DHSC will be extending the strategy to include children. Early in the new year, to inform the DHSC review, they will be launching a national call for evidence to hear the views of autistic people, their families and carers as well as those of professionals. The DHSC want to know what is working and where progress has been made and importantly where they need to push harder to transform the lives of autistic people, their families and carers. DHSC expect to publish their revised autism strategy in November 2019.

The Mental Health of Children and Young People in England, Autism spectrum, eating and other less common disorders topic report 2017 presents the prevalence of autism spectrum disorders, eating disorders, and other less common disorders in 5 to 19year olds in England. A copy of the report is available at: <a href="https://digital.nhs.uk/data-and-information/publications/statistical/mental-health-of-children-and-young-people-in-england/2017/2017">https://digital.nhs.uk/data-and-information/publications/statistical/mental-health-of-children-and-young-people-in-england/2017/2017</a>. Autism Spectrum Disorder was identified in 1.2% of 5 to 19year olds. The prevalence of Autism Spectrum Disorder in 5 to 15year olds remained stable between 2004 (1.0%) and 2017 (1.3%). This rate is also comparable with that found in adults of all ages, as well as in the Avon Longitudinal Study of Parents and Children and the Millennium Cohort Study (Brugha et al., 2016). There is a widespread perception that rates of autism are increasing. However, it is possible that increased reports in clinical practice reflect increased recognition by parents and practitioners, rather than an increase in the number of children with difficulties with social communication and interaction.

However, with regard to the causes of autism, I can only re-iterate that the evidence accumulated on a global level since 1998 provides no support for a role of MMR vaccine, or any vaccine. Your letter refers to comments on individual studies from a Cochrane review, but the key conclusion from that review (available at: <a href="https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004407.pub3/full">https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004407.pub3/full</a>) was that there is no evidence of an association between MMR vaccine and autism (as well

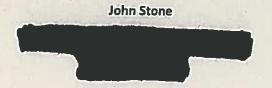
as asthma, leukaemia, hay fever, type 1 diabetes, gait disturbance, Crohn's disease, demyelinating diseases, bacterial or viral infections), and that the existing evidence supports current policies of mass immunisation with MMR vaccine. Any epidemiological study will have its own strengths and limitations, and these are discussed within the individual publications. Numerous studies have been undertaken, using different methods and in different populations, and the findings have been consistent with regard to the safety of MMR vaccination. With regard to the Yellow Card Scheme, the strengths and limitations of any form of passive surveillance are well-known, but this has no bearing on the weight of epidemiological evidence in favour of MMR vaccine safety.

Based on current evidence, there is no rationale on which to re-examine our existing immunisation policy.

Yours sincerely

Say C

PROFESSOR DAME SALLY C DAVIES FRS FMedSci CHIEF MEDICAL OFFICER



Dame Sally Davies,

Chief Medical Officer to the British Government,

39 Victoria Street

Room 75 - 7th Floor

London SW1H 0EU

4 January 2019

Dear Dame Sally,

#### Re: MMR Safety and Autism Numbers

Thank you for your further courteous reply (20 December), however I must point to a host of anomalies (apologies for the length and detail of my reply). The MMR programme was introduced to the UK in 1988 but the earliest of the autism safety studies included in the Cochrane review 2005 [1] was published only a 11 years after this (and by the way was apparently based on illegally obtained children's records, which cannot be cross checked [2]), while the first listed in the review by Luke Taylor, which you cited comes from 14 years after the introduction of the products [3]. Indeed, in 1988 the DH recklessly favoured SKB's Pluserix MMR vaccine although it was already withdrawn in Canada [4] and contrary to your first letter it never made an attempt to withdraw the product until the decision was made to do so unilaterally by the manufacturers in 1992 [5].

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Liam Donaldson, and Prof David Salisbury (who headed the vaccine programme 1986-2013) were capable of suggesting that an infant was capable of receiving thousands of vaccine products in one go without harm [7], which should not perhaps have reflected well on their judgment.

The opposite of side the coin is insouciant denial of any harm at all: it may be that the Department of Works and Pensions has recently been forced by the Court of Appeal to make payments in some Pandemrix/narcolepsy cases having adopted a Catch 22 approach claiming that long term damage could not be assessed [8], but until that point payments had dried up altogether for several years, despite the endless expansion of the programme [9]. In the case of Pandemrix and narcolepsy the MHRA and the EMA failed to pick up signals despite there being a great many [10]. In the general case of vaccines and autism, even if the MHRA paid attention initial adverse events, they would have no machinery to follow up on long term developmental problems: the enduring system is in fact designed not to pick them up. In view of the failure to actively monitor vaccine adverse events and their sequelae the DHSC is not even in a position to say that they are rare. Given, for instance, the current debate over HPV vaccines [11,12,13] what are the ethical grounds for not warning the public, or even continuing to license the products?

By a coincidence the 2017 Mental Health Survey for Children and Young People in England [14] was published the day after I wrote to you. I raise an eyebrow at your suggestion that a 30% rise represents stability, but the survey also deserves to be taken much less seriously than the recent Northern Ireland census [15,16] where there was a proper attempt to count all the cases rather than project numbers from a tiny sample. It is possible that there may have been a few more fringe diagnoses in the 2.9 rate recorded compared with 1.2% 9 years before, but nevertheless Stage 5 diagnoses had all but doubled between 2008-9 and 2017-8, from 0.89 to 1.74%, which makes 1 in 57 children today with a complex ASD impairment. Given innumerable media reports of the system breaking down, and many new facilities having to be provided across the entire United Kingdom this seems to be much more likely to be representative than the results of the new survey [17,18, 19,20]. According to a Haringey budget consultation from January last year [21] the number of adults requiring support with learning disability is set to have risen from 556 in 2013 to 1,147 in 2022 - if the trend continues it looks like it would completely have overtaken the elderly by the later 2020s, but these are cases which unlike the elderly will have a lifetime of dependency ahead of them. Bearing in mind the huge and increasing budgetary constraints on local authorities, it seems improbable that their criteria for recognising new cases has become more lenient. Nor are the figures across the country likely to be much different from those in Haringey I have cited. Since each case is set to cost the state and more important the public millions of pounds, they really ought to be properly counted.

I fear we also need to return to the old data. In the 1999 schools' mental health survey the PDD rate among secondary school children born 1984-88 was 1 in 500 compared with 1 in 250 in primary school [22], but by 2004 survey when virtually all children in school were of the MMR generation the figure hard risen to virtually 1 in 100 across the board [23]. At the time some of us were exercised over claims that any of this was at all normal but now if we look at what was written at the time we are still looking at relatively modest figures. For instance, Gillberg and Wing stated in 1999 [24]:

"The early studies yielded prevalence rates of under 0.5 in 1000 children, whereas the later ones showed a mean rate of about 1 in 1000. There was a marked difference in prevalence rates between those studies that included some children born before 1970 (low rates) and those that included only children born in 1970 and after (high rates). This is probably due to the lower rates obtained by use of criteria strictly based on Kanner's description of his syndrome."

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This was one of the papers that the DHSC sent to reassure me when I first expressed concern about the situation in Haringey in early 2000. But this is a whole order of magnitude different from the current situation, while attempts to locate the missing numbers (as opposed to the occasional case) in a population now over the age of 30 have signally failed. In 2013, in contrast to National Autistic Society projections, of 700,000 cases across the entire population the DWP knew of only 129,000 who were likely preponderantly minors [26]. Brugha's figure for adults in 2009 was extravagantly extrapolated, based on flawed diagnostic methodology and the hypothesis that they had somehow missed nearly 3/4s of the cases before weighting, and was downgraded by National Statistics to the status of "experimental statistics" in 2016 [27], while his 2014 data was published in 2016 as only "experimental statistics" [28]. The "they must be there somewhere" line has been playing for two decades without the cases ever being found. But if they were there, they would be a massively dependent and expensive population and they would not have to be looked for.

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In 2013 you wrote in your Annual Report on another matter [29]:

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- [9] Annex A Vaccine Damage Payments claims received and award statistics, <a href="https://www.whatdotheyknow.com/request/242813/response/599844/attach/3/Annex%20A.pdf?cookie\_passthrough=1">https://www.whatdotheyknow.com/request/242813/response/599844/attach/3/Annex%20A.pdf?cookie\_passthrough=1</a>
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Yours sincerely,

John Stone



Dame Sally Davies,

Chief Medical Officer to the British Government,

39 Victoria Street

Room 75 - 7th Floor

London SW1H OFU

6 January 2019

**REVISED VERSION** 

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According to a recent report the number of young people with learning disabilities held in unsuitable conditions in short term assessment units (but not necessarily for a short stay) has doubled to 2,375 cases in the last three years [21]. A Haringey budget consultation from January last year [22] states that the number of adults requiring support with learning disability is set to have risen from 556 in 2013 to 1,147 in 2022 – if the trend continues it looks like it will completely have overtaken the elderly by the later 2020s, but these are cases which unlike the elderly will have a lifetime of dependency ahead of them. Bearing in mind the huge and increasing budgetary constraints on local authorities, it seems improbable that their criteria for recognising new cases has become more lenient. Nor are the figures across the country likely to be much different from those in Haringey I have cited. Since each case is set to cost the state and more importantly the public millions of pounds, they really ought to be properly counted.

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Yours sincerely,

John Stone



Dame Sally Davies,

Chief Medical Officer to the British Government,

39 Victoria Street

Room 75 - 7th Floor

London SW1H 0EU

18 January 2019

Dear Dame Sally,

## Re: Study limitations and adverse event reporting

Further to your letter of 20 December and my reply of 6 January I note your comment:

"Any epidemiological study will have its own strengths and limitations, and these are discussed within the individual publications. Numerous studies have been undertaken, using different methods and in different populations, and the findings have been consistent with regard to the safety of MMR vaccination."

But it is evident that the six studies in the Luke Taylor "meta-analysis" which you chose to cite while different in kind all had serious shortcomings of both design and reporting, and it is not clear where the good studies are. The papers by Madsen and DeStefano which were commissioned by the Centers for Disease Control and featured in the Institute of Medicine Review of 2004 were also part of a fundamentally flawed process. The parameters of the review were set by Dr McCormick and Dr Stratton at a closed door meeting of the Institute of Medicine in January 2001 which was subsequently published under United States Freedom of Information [1]:

Dr. McCormick: ...[CDC] wants us to declare, well, these things are pretty safe on a population basis (p. 33).

Dr. Stratton: ...The point of no return, the line we will not cross in public policy is pull the vaccine, change the schedule. We could say it is time to revisit this, but we would never recommend that level. Even recommending research is recommendations for policy. We wouldn't say compensate, we wouldn't say pull the vaccine, we wouldn't say stop the program. (p. 74)

Dr. McCormick: ...we are not ever going to come down that [autism] is a true side effect...(p. 97)

There are powerful documentary grounds for believing that the entire process was an exercise in window dressing, and these papers were part of it.

You state:

"With regard to the Yellow Card Scheme, the strengths and limitations of any form of passive surveillance are well-known, but this has no bearing on the weight of epidemiological evidence in favour of MMR vaccine safety."

But the recording of adverse events (or rather the non-recording) may have a great deal to do with certain studies – for instance, the first study by Brent Taylor et al of 1999 [2] which used (apparently without legal sanction [3]) patient records. If events are not recorded – considered too routine or insignificant to bother with - they do not become data: not only are we entirely dependent on Taylor's interpretation (bearing in mind that he prejudicially called Wakefield's theory "crackpot" in the Daily Telegraph [3]) the information would manifestly not be there in the first place.

To emphasise this point in the last decade I complained several times in British Medical Journal Rapid Responses about an NHS culture in which adverse events were routinely ignored, exemplified by the advice on its website "MMR the Facts" [4,5,6] shortly after at the Wakefield affair blew up (it may be noted also that NHS 'MMR the Facts" linked to website of Brian Deer, the journalist who was making allegations against Wakefield [7]):

Q."My son had a sever (sic) reaction to the first MMR jab. Does this mean that he is well protected from these diseases, or is a second dose still necessary?"

A. "If a child has responded to all the components of the vaccine the first time, he will not have a problem being exposed to the viruses again. It's like any one of us who is already immune meeting someone with the disease – the infection can't get established.

"If he hasn't made protection to all three diseases after the first time, then he would still be susceptible to those natural infections, and still needs the 2nd dose.

"Reactions after the 2nd dose are essentially the same as after the 1st dose, but if they do occur they are even rarer. There are no new side effects after the 2nd dose that do not occur after the 1st dose. The advice is therefore that it is safe for your child to have the 2nd dose in order that he is properly protected."

This was no accident: in July 2009 I commented [6]:

"The advice was taken down for a brief period of months in late 2004 early 2005, and then early last year a line was added that you might want to consult your doctor in the event of a severe adverse reaction, but it was changed back again shortly afterwards."

So, it looks as if someone momentarily thought this could be a hostage to fortune but the policy nevertheless went full steam ahead: the NHS paid no attention to severe adverse reactions, and the public were encouraged to dismiss them. This is, I believe, the only reading.

According to a CDC funded paper by Le Baron (2006), for example, as many as 1 in 17 toddlers receiving MMR will get a temperature of 39.5C or more but the follow up period in that study was only 28 days [8]. If this had implications for the medium term development of ASD in children we simply would not know because no one looked - even after all that furore. Given that the core allegations against the Wakefield paper were long ago dismissed in the High Court [9], we can begin to wonder whether the greatest crime of Prof Walker-Smith's team was to collect and collate detailed patient histories. In the end even the public vilification of Wakefield could become a source of research bias.

It is obviously the case — and humanly understandable - when a government policy comes under scrutiny that officials will become defensive, nor is it hard to see how they could fund a multitude of

papers supporting the policy, which might not have supported the policy if better executed (such as several cited in this correspondence), with frankly cracks appearing everywhere. How do we disregard either the conflicts or the flawed evidence?

Meanwhile, our schools are drowning in unprecedented levels of neurological impairment for which we still have no explanation.

All these matters need to be urgently revisited.

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Yours sincerely,

John Stone