# Accelerated Access Collaborative Board Meeting

## Wednesday 23 March 2022 09:00 - 11:00

#### Chair:

Professor Lord Darzi of Denham OM KBE PC FRS (Director of the Institute of Global Health Innovation, Imperial College London)

### **Board attendees:**

Matt Whitty (Chief Executive Officer, Accelerated Access Collaborative and Director of Innovation, Research and Life Sciences, NHS England and NHS Improvement)

Amanda Pritchard (Chief Executive Officer, NHS England and NHS Improvement)

Ben Osborn (President, Association of the British Pharmaceutical Industry)

Professor Chris Whitty (Chief Medical Officer, Commercial and Life Sciences, Department of Health and Social Care (DHSC))

Professor Dame Sue Hill (Chief Scientific Officer, NHS England, and NHS Improvement)

Dan Mahony (Chair, UK BioIndustry Association)

Doris-Ann Williams (Chief Executive Officer, The British In Vitro Diagnostic Association (BIVDA))

Professor Gary Ford (Chair, Academic Health Science Networks (AHSNs))

Professor Helen Stokes-Lampard (Chair, Academy of Medical Royal Colleges (AoMRC))

Jacqui Rock (Chief Commercial Officer, NHS England and NHS Improvement)

Dr June Raine (Chief Executive, Medicines and Healthcare products Regulatory Agency (MHRA)

Lucy Chappell (Chief Scientific Advisor, Department of Health and Social Care)

Luella Trickett (Director, Value & Access, Association of British HealthTech Industries) deputy for Peter Ellingworth

Nicola Perrin (Chief Executive, Association of Medical Research Charities)

Rosalind Campion (Director of Office of Life Sciences)

Dr Samantha Roberts (Chief Executive, National Institute for Health and Care Excellence)

John Stewart (National Director of Specialised Commissioning, NHS England and NHS Improvement)

Dr Tim Ferris (Director of Transformation, NHS England and NHS Improvement)

Dame Ottoline Leyser (Chief Executive Officer, UK Research, and Innovation (UKRI)

Sarah Woolnough (Chief Executive Officer, Asthma UK and the British Lung Foundation; National Voices Representative)

#### **Guest attendees:**

Dan Bamford (Deputy Director Al Award, Innovation, Research and Life Sciences, NHS England and Improvement) *presenter* 

Dr Bola Owolabi (Director Health Inequalities, NHS England and NHS Improvement)

Dr Habib Naqvi (Director of the NHS Race and Health Observatory)

Alex Mclaughlin (Deputy Director, Missions SRO & NHS Innovation, Office for Life Sciences) *presenter* 

Lord Prior (Chair NHS England Board)

### Other attendees:

Georgia Coll (Project Support Officer, AAC, NHS England and NHS Improvement) Secretariat

Lindsey Hughes (Director of Policy, Research and Engagement, IRLS, NHS England and NHS Improvement)

Matthew Newman (Deputy Director, AAC, NHS England and NHS Improvement)

Naomi Miles (AAC Programme Manager, NHS England and NHS Improvement) Secretariat

Pollyanna Jones (Chief of Staff, AAC/IRLS, NHS England and NHS Improvement)

Steve McAteer (Advisor & Private Secretary to Lord Darzi)

Sutharsan Satkunarajah (Advisor to Lord Darzi; Imperial College London)

## **Apologies:**

Peter Ellingworth (Chief Executive, Association of British Health Tech Industries (ABHI)) Professor Chris Whitty (Chief Medical Officer, Commercial and Life Sciences, Department of Health and Social Care (DHSC))

Dr Louise Wood (Director, Science, Research & Evidence, Department of Health and Social Care (DHSC)

## **Summary of actions**

#	Action	Owner	Due Date
1	Board members to email any comments on the papers to note to the AAC team at aac.innovation@nhs.net.	All	30 March 2022
2	Professor Helen Stokes-Lampard to introduce Matt Whitt and Gary Howsam, Vice Chair, Royal College of General Practitioners (RCGP)	Helen Stokes- Lampard	31 March 2022
3	Matt Whitty to provide an update to the AAC members on the development on the complex transactions approach at future Board meeting.	Matt Whitty	30 Nov 2022
4	OLS to be involved in Health Inequalities work led by IRLS team to ensure alignment with LSV Missions.	Matt Whitty / Rosalind Campion	29 June 2022
5	Rosalind Campion to provide an update on funding allocation against each LSV mission at the next Board	Rosalind Campion	29 June 2022

Note: These minutes are a summary record of the main points discussed at the meeting and the decisions made. They are not intended to provide a verbatim record of the Board's discussion.

## 1. Welcome and introductions

- 1.1 Lord Darzi welcomed the following new board members:
  - Dr Tim Ferris (Director of Transformation, NHS England and NHS Improvement), replacing Matthew Gould and Hugh McCaughey
  - Jacqui Rock (Chief Commercial Officer, NHS England and NHS Improvement)
     Commercial representative for NHS England
  - Dr Samantha Roberts (Chief Executive, National Institute for Health and Care Excellence), replacing Gillian Leng.
  - Dan Mahony (Chair, UK BioIndustry Association), replacing Dr Ruth McKernan
  - Lucy Chappell (Chief Scientific Advisor, Department of Health and Social Care), replacing Steve Oldfield
  - Rosalind Campion (Director of Office of Life Sciences), replacing Kristen McLeod
  - Nicola Perrin (Chief Executive, Association of Medical Research Charities), replacing Aisling Burnard
- 1.2 Apologies were noted from Peter Ellingworth, Louise Wood and Chris Whitty.
- 1.3 The following guests were welcomed:
  - Lord Prior (Chair NHS England Board),

- Dr Bola Owolabi (Director Health Inequalities, NHS England and NHS Improvement),
- Dr Habib Naqvi (Director of the NHS Race and Health Observatory),
- Dan Bamford (Deputy Director Al Award, Innovation, Research and Life Sciences, NHS England and Improvement) and
- Alex Mclaughlin (Deputy Director, Missions SRO & NHS Innovation, Office for Life Sciences).
- 1.4 Lord Darzi expressed gratitude on behalf of the Board to Ben Osborn for his contribution and support and Louise Wood who has been instrumental to the NIHR and ally to the Board. The Board wishes them both well in the future,
- 1.5 There were no conflicts of interest declared.
- 1.6 There is one additional paper (paper 7) for the Board to note which will not be presented at this meeting.

#	Action	Lead	Deadline
1	Board members to email any comments on the papers to note to the AAC team at aac.innovation@nhs.net by 30 March 2022	All	30 March 2022

## 2. Review of previous minutes and actions

- 2.1. The previous minutes were accepted by the Board as an accurate record of the previous meeting.
- 2.2. Matt Whitty noted the following three open actions from the previous meeting, all of which are ongoing.
  - Gillian Leng and Alison Austin to ensure NICE are linked into the work of the IRLS Research Team to embed research in the everyday work of the NHS – This action remains open and to be taken forward by Sam Roberts
  - Discussion around novel payment methods for ATMPs to be progressed outside of the AAC Board
  - Julia Dudley (OLS) to provide an update on how medical research charities who are not explicitly mentioned in the healthcare missions engage with the allocation of the CSR funding. Alex Mclaughlin provided the following statement: "Medical Research Charities will be critical to the delivery of all the Healthcare Missions, and there is already active engagement on several them. Where Medical Research Charities would like to be involved in any of the Missions (whether Cancer, Dementia, Obesity, Addiction, Mental Health, Ageing, Vaccines or Respiratory), they are invited to contact Alex Mclaughlin, the Office for Life Sciences Deputy Director for Innovation and Growth, on <a href="mailto:alex.mclaughlin@beis.gov.uk">alex.mclaughlin@beis.gov.uk</a>, to discuss further."
- 2.3. All other actions have been closed.

## 3. AAC CEO Update

- 3.1. Matt Whitty updated the board on the new programme report format which has been refreshed to reflect our focus on the five AAC priority areas and the crosscutting work agreed by the AAC Board. The programme report has been refreshed and refined to give the Board the most relevant information to conduct its business. There is an ongoing piece of work to further redesign and refresh how we report the impact of our work. Matt welcomed feedback from Members on the new format and approach.
- 3.2. Matt provided a verbal update on key highlights across IRLS:
- 3.3. Matt shared his reflections from the Academic Health Science Networks (AHSNs) tour, which has restarted after a pause due to Omicron. Matt and team have visited 11 of the 15 AHSNs and met with numerous innovators, Integrated Care Systems (ICSs) and providers being supported by the AHSNs and heard more about the plans for working with ICSs in the future. Matt noted that it had been great to have Board members and their teams join the tour and encouraged those who had not yet attended to join the remaining sessions if possible.
  - Lord Darzi noted the significant contribution of AHSNs throughout COVID-19.
  - Lord Prior reflected that the role of AHSNs in driving adoption and spread is not sufficiently clear, particular in primary care. We are good at innovating but not adoption and spread. The example of Babylon was used, the primary care model was proven in the UK but couldn't be scaled up, it is now a \$bn business in the US. Lord Prior challenged members to consider what we can do nationally to leverage local spread.
  - Lord Darzi noted the absence of primary care in US, introducing Babylon created a new service opposed to replacing or redesigning an existing one, but agreed the point remains.
  - Rosalind Campion reinforced Lord Prior's point, supporting the need to reinforce a collective understanding of the roles and responsibilities of the AHSNs, ensuring a common understanding across industry, government, and NHS to avoid any mismatched expectations.
  - Gary Ford reflected on the relationships between ICSs and AHSNs, they are
    developing well but vary depending on the maturity of the ICS. Joint working
    models have been developed and learning has been shared with Matt and the
    team. Gary confirmed that the AHSN are clear on their role in spread and
    adoption for NHSE commission but recognised that more levers are needed
    in primary care. The AHSN are already working in primary care particularly
    around transitioning care from secondary into primary care i.e. innovation in
    community diagnostics.
- 3.4. Matt presented the Impact Data to the Board. Compared to the position at Q3 last year (2020/21), the AAC is supporting a greater number of innovators and innovations with an increase of over 300k. Savings are also up from £19m to £74m compared to last year.
  - Matt advised that we continue to report our impact but will focus reporting on a smaller number of national programmes. We have been dramatically underestimating our impact, and committed to bringing an updated scorecard to a future AAC Board
  - Lord Darzi added the merit of provider organisations being able to claim ownership of these savings and welcomed more granular data on these savings.

- 3.5. Matt presented the newly formatted programme progress report which includes a progress rating against each priority.
  - Demand signalling and Horizon Scanning: Decision to increase resource and focus for these processes, developing closer links with national clinical programmes in policy development and local systems.
  - Research: Continued work on research prioritisation including publication of Excess Treatment Cost guidance. The next phase of National Contract Value Review to be launched in April 2022. Continued support for the Research Resilience and Growth programme with National Institute for Health Research
  - Uptake of NICE-approved products:
    - MedTech pathway has been mapped from ideation to adoption and spread, a paper to the Board provides an overview of the steps innovators should go through and highlight opportunities for improvement,
    - ii. **Medicines pathway mapping initiated following the approach** taken to map the MedTech pathway,
    - iii. **Al Health and Care Award:** Round 3 winners have been agreed by the Al Lab Board with the anticipated announcement in June.
    - iv. **Rapid Uptake Products:** Significant work has been undertaken to pivot the RUPs to focus on the clinical areas of CORE20plus5,
    - v. **Support for NICE approved Lipid Therapies:** Good news for the high intensity statin and ezetimibe with an extra 350k and 17.5k patients respectively. Uptake of Inclisiran is slower than expected, NHSE are supporting local systems with guidance and implementation tools. New cohorts for CEP and NIA to be announced.
    - Workforce and local systems: We are moving towards re-licensing AHSNs with a renewed focus on Health Inequalities, linking more proactively into ICSs and research infrastructure to increase impact. New cohorts for Clinical Entrepreneur Programme and NHS Innovation Accelerator have both been announced this quarter.
    - **Collaboration**: Innovation Service remains in private beta, ahead of Support Organisation Agreements being signed.
    - Cross-cutting: A proposal to adapt, expand or refocus several the
      programmes so that they better align with the strategic approach to
      addressing HI articulated through the NHS Core20PLUS5 is set out in a
      paper to the Board.
- 3.6. Matt advised the board that uptake of Inclisiran has been slower than expected.
- 3.7. Lord Darzi asked what lessons can be learnt from Inclisiran considering it is a major national deal?
- 3.8. Matt advised that a new primary care focused model had been introduced by that is was still early days, NICE approval was received 1<sup>st</sup> September 2021. He also reflected on the challenges engaging relevant partners during the pandemic. A strong plan and incentives in primary care are in place but remains a challenge.
- 3.9. Professor Helen Stokes-Lampard directed the team to work with Royal College of General Practitioners (RCGP) directly and offered to make an introduction to Gary Howsam, Vice Chair.
- 3.10. Gary Ford advised earlier engagement with secondary care as well as primary care.

#	Action	Lead	Deadline
2	Professor Helen Stokes-Lampard to introduce Matt Whitt and Gary Howsam, Vice Chair, Royal College of General Practitioners (RCGP)	Helen Stokes- Lampard	31 March 2022

## 4. How AAC partners are Addressing Health Inequalities

- 4.1. Matt Whitty introduced the paper which sets out the proposals to adapt, expand or refocus several the programmes currently being delivered by the AAC Delivery Unit. This is so they better align with the strategic approach to addressing health inequalities articulated through the NHS Core20PLUS5 approach. It sets out early detail on these changes.
- 4.2. The paper considers the following areas in more detail:
  - Implications for the work of the AAC and its delivery unit
  - Plans to achieve it
  - The AAC's commitment to tackling health inequalities
- 4.3. Matt expressed his enthusiasm about the paper and on-going work in collaboration with Dr Bola Owolabi and the Health Inequalities Directorate
- 4.4. Matt explained how the selection process for next round of RUPs has been a driver for the refocus, following a long robust selection process three technologies were identified None of the technologies were strategically aligned to our priorities or big enough scale.
- 4.5. Matt asked to Board to consider the approach set out in this paper.
- 4.6. Due to technical issues for Bola, Matt presented the Core20PLUS5. <a href="NHS England">NHS England</a> <a href="NHS England">NHS England</a>
- 4.7. This approach has clear alignment the AACs work:
  - AHSNs are supporting ICS to identify evidence-based solutions for each of the Core20Plus5 clinical areas.
  - Refocusing IRLS national programmes including Rapid Uptake Product (RUP), Small Business Research Initiative (SBRI) etc. on Health Inequalities challenges
- 4.8. Habib Navqi was invited to introduce the NHS Race and Health Observatory (NRHO) and comment on the paper. NRHO was established by NHSE as an 'armslength' organisation, intended to act as a critical friend to drive research, policy recommendations and support system implementation of policy. Habib highlight two longstanding issues 1) increased use of digital innovation such as app, understanding whether those apps help to reduce, not increase health inequalities and, 2) representation in clinical trials for genomics. Habib acknowledged the need to review the capabilities and skills of our leaders and infrastructure to address HI through innovations
- 4.9. Lord Darzi thanked the team for the paper and highlighted its importance and strong focus on the right questions.

- 4.10. Samantha Roberts offered NICE support and expertise with this programme and have mapped guidelines to the five areas which they are happy to share. She said that for diagnostics, digital and technology, they have historically waited for industry to approach them. Going forward, NICE are looking to AAC partners to identifying the most important innovation for them to access
- 4.11. Lord Prior was in support and keen to ensure this work is aligned with LSV Missions. He requested Rosalind is involved in this, to ensure total alignment. Matt agreed with this request, confirming maternity is probably the only area where there is not alignment.
- 4.12. Ben Osborn agreed with Lord Prior emphasised the need to give a consistent and clear message to industry as to where our priorities are in the UK. He raised a question regarding the gap and risk for the existing RUPs and where this change of direction leaves them. The term "pause" is used within the report and it would helpful to understand whether this is temporary or permanent. He also queried the reference to the "Triage Board" detailed in the report and the governance and membership of such Board.
- 4.13. Matt advised that the Board would need to decide on what "pause" of RUPs means. It could be a stop, but alternatively RUPs may be repurposed in the future, depending on the outcome of this work. This will be reconsidered at a future Board following the MedTech and Medicines Pathway work. In relation to the triage
- 4.14. In relation to the triage approach for complex transactions, he explained they are currently working with the commercial department and commercial medicines directorate to finalise the arrangements it and a summary will come back to future Board.
- 4.15. Sarah Woolnough supported the approach and change of direction. She asked how the AAC can support sharing best practice and lessons learned from COVID-19
- 4.16. June Raine expressed support from MHRA. She welcomed thoughts on possible changes to the regulatory framework for medical devices, that could potentially act as a lever for increasing representatives. She asked what data there is for showing impact, and how we capture ethnicity and methodological approaches to address bias.
- 4.17. Lucy Chappell voiced support for the new direction. She raised the challenge that areas with high clinical workload and high disease burden do not have capacity for R&I and it should be considered how we bolster support where there could be greatest impact. This work needs strong links to the LSV and a coordinated workforce piece. She echoed previous comments on the importance of capturing evidence and metrics,
- 4.18. Sue Hill echoed points made by Sarah, Lucy and June. In response to Habib's point on genomics, she acknowledged the need to focus on getting more data on who is accessing genomic test testing. Genomics England are looking specifically at the level of diversity in the national research database to enable algorithms to make the data suitable to the national population.
- 4.19. Matt thanked the Board for their support.

#	Action	Lead	Deadline
	Matt Whitty to provide an update to the AAC members on the development on the complex transactions approach at future Board meeting.	Matt Whitty	30 Nov 2022

4	OLS to be involved in Health Inequalities work led	Matt Whitty /	29 June 2022
	by IRLS team to ensure alignment with LSV	Rosalind Campion	
	Missions.	·	

## 5. MedTech Pathway Mapping Work: Innovation from Bench to Bedside in the NHS

- 5.1. Luella Trickett introduced the paper and the value of revisiting the MedTech pathway. She recognised that funding is big challenge and historically we have not been good as spending to save. Understanding these barriers will lead to system change.
- 5.2. Dan Bamford presentation the paper, explaining that this work was a timely refresh of the work that was the genesis of the AAC. The work details an idealised set of steps that a MedTech innovator would take from ideation to adoption. It has been useful to re-baseline our understanding of the process and the challenges within it. It has been beneficial to target the work of the AAC and understand if we are putting AAC resources against the challenges in the pathway that will have the biggest differences for patients. It also provides an intellectual framework for prioritising future work.
- 5.3. A further benefit will include communicating the outputs of this pathway with innovators which will help them better prepare for accessing the market. It is intended that this will lead to valuable conversations, where we can share the information more transparently, through the Innovation Service. It will also provide a framework to help consider future work and programmes.
- 5.4. 26 steps have been identified which talks to the complexity of the pathway and challenges partners will recognise
- 5.5. Dan asked the Board to endorse the approach and invited Board members to be involved in planned workshops
- 5.6. Doris Ann Williams, Nicola Perrin and Samantha Roberts all agreed to co-host a session.
- 5.7. Matt Whitty said that this is a detailed piece of work and thanked all of those involved. He shared the experience introducing placental growth factor (PIFG) testing from two sites to all sites. This was achieved by building each step at a time, on a learning 'as we go' basis. This is not efficient. This work will help us take a strategic view and design systematic solutions.
- 5.8. Rosalind Campion showed support from OLS, agreeing that the pathway is hugely important. She highlighted there may be some research and development funding to support system-wide approach.
- 5.9. Gary Ford raised that adoption and spread strategies need to be thought about earlier in the pathway. We also need to consider how this is shared with Industry. He thanked Matthew Robinson from IRLS who is leading the mapping work.
- 5.10. Tim Ferris said it is great to have a pathway and steps and these generalisable and not dissimilar in the US. He cautioned not to lose sight of the major barriers. The biggest barrier is proof of concept into operations, balancing delivery of care innovation. The role of management/operations should not be overlooked.
- 5.11. June Raine said there is a significant opportunity simplify clinical through changes in regulatory framework. We need to simplify trials and ensure international compatibility taking advantage of Brexit.
- 5.12. Ben Osborn welcomed the paper and reflected that many of the issues identified also apply to medicines, so it would be beneficial to consider them in parallel.

- 5.13. Sue Hill feedback on yesterday's roundtable where the need to review the commissioning landscape for diagnostics and look at levers to support diagnostic uptake was identified. There is a need to align the commissioning system with the technology. A key question is how we adopt MedTech at scale in a systematic way as in the NHS.
- 5.14. Lord Darzi thanked the presenters for a good paper and said he would advocate clinical leadership at a local level. He said we need to find ways of engaging and support clinicians and to make it easier for them

# 6. Delivery of the Life Science Vision Healthcare Missions

- 6.1. Lord Darzi gave a foreword to the paper, emphasising its critical importance given the life science history of the UK. He invited Lord Prior's to introduce the paper.
- 6.2. Lord Prior spoke to how the NHS has become a late stage sickness service which is being overwhelmed and cannot cope with the burden of sickness. This is evidenced by life expectancy falling and inequalities rising. Advancements in sciences and emerging technology present an opportunity of a new model of care, which is at the core of the Life Science Strategy. The three missions laid out in the paper whereby intervening at an early stage and in a more personalised way we can have a huge impact. The future vision should be healthcare rather than sick care.
- 6.3. Alex McLaughlin presented the paper. The paper describes the plans for the delivery of The Life Science Vision. This Vision was published in July 2021, and set out Government, the NHS and Sector's plans for making the UK the globally leading location for Life Sciences over the next decade.
- 6.4. The Vision details eight Healthcare Missions, which have been designed to build on the success of the UK's Vaccine and Research response to the pandemic and apply it to other areas of clinical need.
- 6.5. The Office for Life Sciences have identified the NHS having a fundamental role in the delivery of 3 of the Missions and the specific NHSE and AAC roles will be discussed at a future AAC Board. These are:
  - 1. Mental Health
  - Obesity
  - Cancer
- 6.6. Lord Darzi said there is a need for the focus to shift to becoming global leaders in preventing disease. He referred to the issues listed in the paper as slow pandemics which need tackling. He added that this Board should be focused on investing in prevention and diagnostics which will be key for the future.
- 6.7. Samantha Roberts explained that it would be beneficial to understand how NICE can understand the priority innovations emerging from the missions, so they can be are poised to take them through assessment. Priority diagnostics, devices and digital technologies emerging from the mission work will be important to surface.
- 6.8. Lord Prior said that genomics is becoming a hugely important part of health, which the UK has a lead on. The combination of genomic data, longitudinal health data and the growth of AI will enable personalisation of public health, which will radically drive change in healthcare. The NHS is uniquely incentivised to keep people healthy in a way no other country is. Our future health and UK biobank are great step forwards.
- 6.9. Rosalind Campion added the following notes of caution; underestimating the international competition, ensuring all missions are funded and the four preconditions for success. She expressed gratitude for support given.

- 6.10. Lucy Chappell agreed that the issue of funding should not be overlooked. It is therefore important to have a partnership approach and commitment to working together. We need to consider how we get added value from the money we already have.
- 6.11. Tim Ferris said that the "what" is set out nicely in the paper but the "who" needs further clarity. Focus on working together across organisation. That is where the power and the challenge is.
- 6.12. Sue Hill added that the requirement to invest in workforce and new types of workforce should not be overlooked.
- 6.13. Lord Darzi concluded that the US is now ahead in many areas, such as predictive healthcare and AI.
- 6.14. Matt Whitty queried the OLS budget dedicated to this. Rosalind said that allocations have not been made so far but will speak to Matt and Samantha about finalising decisions.
- 6.15. Lord Darzi thanked Members for the rich discussion.

#	Action	Lead	Deadline
5	Rosalind Campion to provide an update on funding allocation against each LSV mission at the next Board	Rosalind Campion	29 June 2022

#### 7. NHS Genomic Medicine Service and the NHS GMS Research Collaborative

- 7.1. Lord Darzi highlighted that this is at a critical stage of the overall mission and invited Sue Hill to present this paper.
- 7.2. Sue provided an overview of the paper and updated on the NHSE board decision to agree to significant investment in Genomics, including whole genome sequencing (WGC).
- 7.3. The paper sets out how Industry and academia can work collaboratively with NHSE and Genomic England including access to genomic research library to speed up evidence generation and enable rapid approval and adoption of products.
- 7.4. Sue invited the board to consider other areas in the NHS where we should be replicating this model.
- 7.5. Lord Darzi thanked Sue and complimented her on a great paper. He asked Sue to consider how the AAC Board can assist and drive contemporary public health. He expressed gratitude to Sue for her leadership and acknowledge the scale of what has been achieved.

## 8. AOB

- 8.1. No further comments from the Board.
- 8.2. Lord Darzi thanked Members and attendees and closed the meeting.

Next AAC Steering Group meeting is 1 June 2022 at 9:00 – 11:00 Next AAC Board meeting is 29 June 2022 at 09:00 – 11:00