Triple jeopardy: old age, frailty and diabetes in COVID-19

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Abstract

The COVID-19 pandemic has turned the lives of people throughout the world upside down and the virus has hit the older population hardest of all. The term 'triple jeopardy' has been coined to identify that older people with frailty and diabetes are at particular risk from the virus.

Government figures for non-COVID deaths from March to May 2020 show a 20–50% increase in those >70 years but lack of testing capacity may have led to under-reporting of the virus. There has undoubtedly been a catastrophe in care homes, with 40% of total COVID-19 deaths occurring in this setting. Whether frailty poses a greater risk than age alone is uncertain, with observational studies producing conflicting results. NICE guidance to include assessment of frailty in clinical decision making may have introduced study bias.

Diabetes adds additional risk, with 33% of all hospital deaths occurring in people with diabetes: hazard ratio 3.51 for type 1 diabetes and 2.03 for type 2. The majority of those who died were >70 years (60.9% type 1 and 79.2% type 2). Poor glycaemic control is associated with increased risk.

A 19th century definition of triple jeopardy defined gender, race and poverty as the dominant factors and these remain just as relevant in the COVID-19 era. The arrival of a second wave highlights the need to introduce measures to protect people with diabetes and those marginalised by society. This includes older people and their carers.

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Key words

COVID-19; age; frailty; diabetes; triple jeopardy

COVID changes everything

Who, at the beginning of 2020, could have predicted the consequences of the COVID-19 pandemic? These have been truly global, from threats to the existence of Amazonian tribes to the virtual elimination of such sophisticated industries as aviation and hospitality. COVID-19 has penetrated every conceivable aspect of our lives and we hear new facts (and misinformation) about the behaviour and effects of the virus every day. Studies are published without peer review and although vast amounts of information are available, there is still much to be learned. Some facts emerged at the outset: older people are especially vulnerable together with ethnic minorities and those with certain long-term conditions, including diabetes; obesity and deprivation are associated with worse outcomes. People in care homes account for 40% of the total deaths from COVID-19[1] and the reasons behind this disgraceful national statistic have yet to be fully investigated.

In an illuminating article, Sinclair and Abdelhafiz[2] coin the phrase 'triple jeopardy' to describe how old age, frailty and diabetes operate cumulatively to increase the threat to an individual with COVID-19. These inter-related factors lead to poor outcomes, in particular impaired immunity causing increased progression to septic shock and multiple organ failure. Nursing home residency is a proxy for frailty with evidence to suggest that the prevalence of diabetes in care homes is up to 25%.[3]

In this article we look at the risks associated with the combination of age/frailty/diabetes and COVID-19 along with the additional risk of living in an institution, where the triple jeopardy of old age, frailty and diabetes is seen in the harshest light.[2]

The human cost of COVID-19

Case history

Susan's 86-year-old mother, Cynthia, has dementia and lives contentedly in a care home. Susan visits very regularly until the COVID-19 outbreak, when visitors are banned and residents confined to their rooms. Cynthia is able to wave to Susan from a window but as time goes on, it is clear that she is becoming more distracted and distressed. Attempts to communicate with her remotely are unsuccessful – she cannot recognise her daughter during a Facetime call and her ability to converse on the telephone is limited. Her dementia worsens, she becomes disorientated and she is clearly very unhappy.

A resident discharged from an acute unit imports COVID-19 to the care home and despite all efforts to isolate residents, Cynthia contracts the virus. Susan is extremely distressed that she is not allowed to visit and support her ill mother and although Cynthia believes the carer who nurses her is Susan herself, this is of no comfort to Susan, who is devastated that she has been deprived of her rightful place at her mother's side during her final illness. The funeral is limited by COVID-19 restrictions, with no opportunity to celebrate Cynthia's life.

Susan is very angry that the sacrifices made by both her and her mother in the interests of safety, were in vain. Not only was her mother not protected from the virus but she lived her last weeks in a distressed state, unsupported by her family.

At the time of writing, worldwide COVID-19 deaths are 1.15 million (25 October 2020) and many of these casualties, like Cynthia, will have died in a hospital or care home, isolated from the comfort of their family. Relatives are left emotionally scarred and often very angry because their dearly loved relation died 'on their own'. For some, these traumatic bereavements will lead to serious psychological damage. This is not to downgrade the way that nurses and carers have, out of necessity, taken on the role of 'family member' at the time of death, followed by the heart-rending task of breaking the news to their next of kin. The need to perform these difficult tasks day after day does not make them any less distressing and news reports have allowed battled-hardened senior nurses and consultants to describe the emotional strain as unbearable. Let us hope that the weekly applause for front line NHS workers gave them some sense of pride in their perilous work.

For any person 'left behind', grief is compounded by the limitations placed on the funeral. All close contact (hugging) is forbidden and numbers are strictly limited so a 'good send-off' becomes impossible, minimising the support and comfort that someone in grief would expect in normal times.

The impact on the grieving process is even greater in some religious communities, where relatives normally take part in rituals such as washing and shrouding the body, and of course praying for the dead. After burial, there may be an obligatory period of mourning, when friends traditionally come to the home to comfort the grieving family. Such gatherings are all impacted by COVID. The British Board of Scholars and Imams has produced practical guidance for simplifying the burial rituals of the Muslim faith in response to COVID-19 restrictions.[4]

The grief caused by the curtailing of these time-honoured rituals may go unrecognised outside the close family group but adds to the suffering felt by the bereaved with potential for serious psychological consequences.

Age range (years)	Percentage change in non-COVID death rate
10–29	>50% reduction
30–49	20% reduction
50–69	No change
70–89	20–40% increase
>90	Up to 50% increase

Table 1. Office for National Statistics. Analysis of death registrations not involving COVID-19, England and Wales from 28 December 2019 to 1 May 2020, compared with the previous 5-year average for deaths in the same weeks[5]

Non-COVID death rates in older and younger people

From the onset of the pandemic in early March until the start of May 2020, non-COVID death rates show a surprising pattern with the expected high death rates in those over 70 years but significantly reduced death rates compared with the previous five-year average, in people under 50. (Table 1.)

The explanation for the lower death rate in younger people at the start of the pandemic is not obvious and further information may emerge when the detailed breakdown for 2020 is released.[5] National statistics from 2016 record the four main causes of death between age 10 and 35 years as suicide, transport accidents, homicide and accidental poisoning for men, and suicide, transport accidents, accidental poisoning and brain/breast cancer in women. The empty roads during lockdown explain the fall in transport accidents but could reductions of death in men result from the closure of hospitals to non-COVID events? There is precedent for this: during the hospital strikes in Israel in 2000,[6] death rates fell significantly and this statistic remains unexplained.

COVID-19, age and frailty

The simple government message is that older people die of COVID-19 and the young are protected from its ravages. There are exceptions, such as the report from Texas of a 30-year-old man, who died after going to a COVID party to test his belief that the pandemic was a hoax.[7]

If we stick to the WHO definition of Old Age, those over 65 years should be cautious about contracting the virus. Daily government briefings reinforce the message: COVID Kills Old People. However, there is widespread understanding that chronological age is trumped by frailty. Captain Sir Tom Moore chose to

celebrate his 100th birthday by flying in the face of frailty and walking round his garden in support of the NHS. He raised more than £33 million (plus £6 million through Gift Aid) and became a national hero, receiving over 150,000 cards, a birthday salute by a Spitfire and a Hurricane and a knighthood from the Queen.

The significance of frailty, and the need to recognise it, has led to modification of the primary care Quality and Outcomes Framework targets to take frailty into account.[8] Frailty is defined as 'a distinctive health state related to the ageing process in which multiple body systems gradually lose their in-built reserves'.[9] It may manifest itself as physical disability from comorbidities or as cognitive failure and is associated with higher risk of death. If we accept this increased risk in frail older people, it seems logical to extrapolate that frailty also increases the risk of death from COVID-19 – but does the evidence support this assumption? NICE comes down firmly on the side of frailty as the main factor in determining the appropriate degree of medical intervention[10] and recommends that every older person admitted to hospital should have a frailty assessment.[11] This approach is supported by an observational study conducted at 10 UK hospitals and a single Italian hospital, which concluded that 'disease outcomes were better predicted by frailty than either age or comorbidity'.[12] However, if clinicians hold the belief that frailer patients with COVID-19 have less favourable long-term prospects and are thus less deserving of invasive treatment, this becomes a self-fulfilling prophesy and the outcome is influenced by medical bias.

Evidence from other studies suggests that age, rather than frailty, is the dominant risk factor. A study of admissions of people aged >70 years to a central London hospital compared mortality rates in 217 people with COVID-19 and 160 people without the virus. In the COVID-negative patients, frailty was associated with increased mortality, as expected, but in the COVID-positive cohort, mortality rates were similar, indicating that non-frail patients were equally vulnerable to the virus.[13] (Figure 1.)

A comparable study from Leicester also showed no association between frailty and mortality in older people with COVID-19.[14] The authors of these studies put forward possible, but differing, explanations for their findings, both related to immunosenescence. These are: (a) frailty may reduce the cytokine storm so that the deaths in frail people relate to the direct effect of the virus;

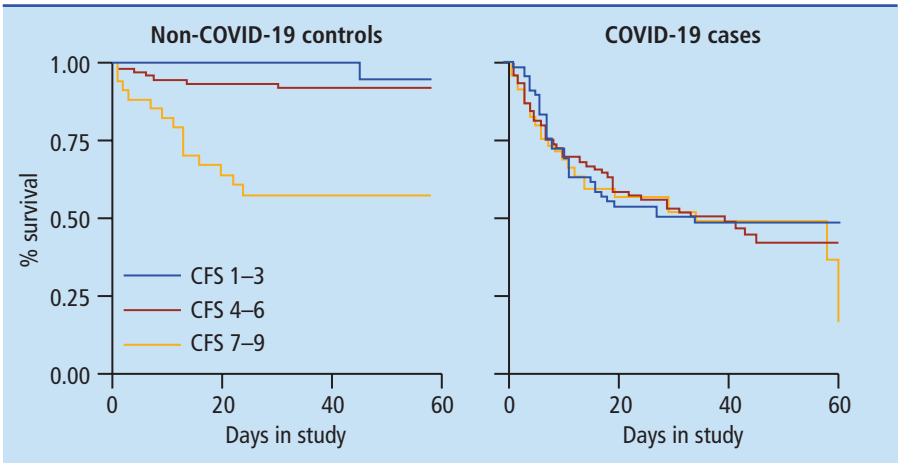

Figure 1. Kaplan-Meier curves showing 60 days survival by tertiles of Clinical Frailty Scale (CFS) and COVID-19 status. (Reproduced from: Miles A, *et al. Eur Geriatr Med* 2020;11[5]:851–5)[13]

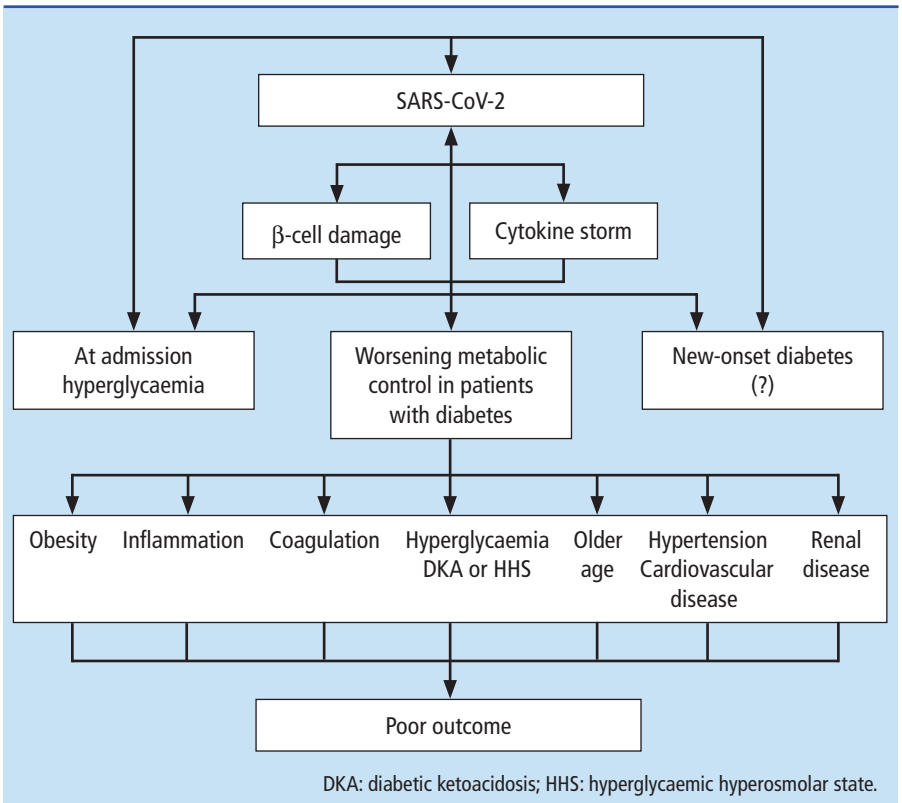

Figure 2. Synopsis of the reciprocal effects of diabetes and COVID-19. (Reproduced from: Apicella M, *et al. Lancet Diabetes Endocrinol* July 17, 2020)[15]

or (b) the cytokine storm may induce rapid onset of frailty in older people who were previously healthy. So the jury is out on the intuitive belief that frailty is related to a higher COVID death rate.

COVID-19 in diabetes and old age

A recent review covers all aspects of diabetes and COVID-19,[15] including potential prognostic factors. In summary, diabetes does not increase the risk of contracting COVID-19 but, once infected, those with diabetes have a higher risk of more serious illness, need for intensive care and death. The increase in morbidity and mortality is related to a number of risk factors linked to diabetes, including obesity, a hypercoagulable state and increased inflammatory markers – the latter associated with the cytokine storm.[15] (Figure 2.) Diabetes complications (particularly cardiovascular disease and renal impairment) increase the risk of vascular episodes. Acute complications such as diabetic ketoacidosis (DKA), occurring in people with both type 1 and type 2 diabetes, or hyperglycaemic hyperosmolar state (HHS) can be very difficult to treat, with reports of extreme insulin resistance. Fluid replacement can also be difficult, particularly in the frail and those with heart failure. People not known to have diabetes but with hyperglycaemia on admission have a higher mortality than those with pre-existing diabetes.[16] The COVID-19 virus has a tropism for the beta cell which may explain the high rates of DKA and HHS reported from the UK[17] and China.[18]

Two recent articles in *The Lancet Diabetes and Endocrinology* based on data collated by the National Diabetes Audit have provided detailed information about the impact of diabetes and age on in-hospital COVID-19-related mortality and on the risk factors for mortality in a population based cohort.

In-hospital COVID-19-related mortality figures from 1 March to 11 May 2020 showed that one-third of people who died with COVID-19 had diabetes.[19] The odds ratio for mortality in type 1 diabetes was 3.51 (95% confidence interval 3.16–3.90) while that for type 2 was 2.03 (1.97–2.09). Age was a significant factor, with 60.9% of those with type 1 diabetes aged 70 years or over, compared with 79.2% of people with type 2. (Figure 3.) The relative impact of diabetes was greater in younger (less than 70 years) vs older people (OR 6.89 vs 2.81 for type 1 diabetes and 3.74 vs 1.79 for type 2) but the absolute number of deaths in the younger cohort was small.

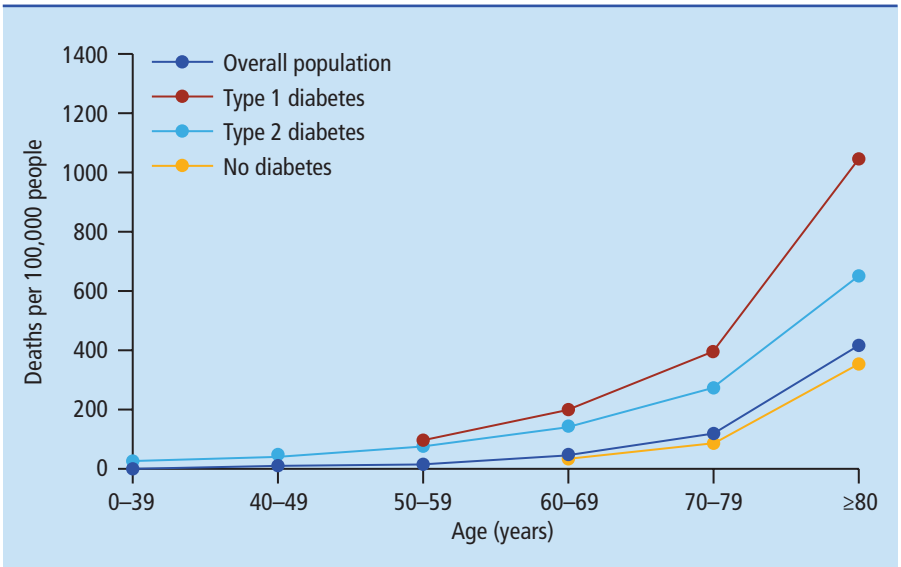

Figure 3. Unadjusted in-hospital COVID-19 mortality rates, 1 March to 11 May 2020, by diabetes status. (Reproduced from: Barron E, *et al. Lancet Diabetes Endocrinol* Aug 13, 2020)[19]

The companion population-based study of risk factors for mortality[20] found a significant increase in death registrations for people with diabetes over a six-week period during April and May 2020 compared with the previous three years. For both type 1 and type 2 diabetes the risk factors were male gender, age, renal impairment, ethnicity, deprivation, and previous stroke or heart failure. Poor glycaemic control (HbA1c 48–53mmol/mol vs 86mmol/mol; 6.5–7% vs 10%) increased the risk for both type 1 (HR 2.23) and type 2 (HR 1.61) diabetes. However, the gradient of the risk association was steeper in those under 70 years of age. Thus, the impact of age outweighs the impact of diabetes on mortality.

The care home catastrophe

Care home residency is a surrogate for frailty[2] and most residents have comorbidities such as hypertension, vascular disease, dementia, depression, arthritis and diabetes.[21] While the government promised 'to throw a protective ring around care homes', the number of deaths in care homes had risen by 50% compared with previous years within two weeks of the national lockdown on 23 March.[22] (Table 2.) So far, there have been no official analyses for these figures. It is relevant that the number of deaths ascribed to non-COVID causes invariably exceeded COVID deaths, even at the peak of the pandemic. The high non-COVID death rate suggests that true fatalities from COVID were not registered as such. Since testing for COVID-19 was restricted to hospital patients at that time, doctors may have been unwilling to confirm the diagnosis on a death certificate without the evidence of a positive test.

There may be other reasons for the high mortality among 'non-COVID' residents of care homes. Isolation of residents, in order to lessen the risk of contagion, carries its own risks. People with dementia, confined to their room with only a carer providing meals and nursing care, may understandably feel they

Date	Deaths from COVID-19	Non-COVID-19 deaths	Deaths in 2019
23/03/2020*	26	421	340
06/04/2020	274	738	373
17/04/2020**	540	666	391
04/05/2020	308	291	338
01/06/2020	89	291	338
*Date of national lockdown. **Peak of COVID-19 deaths.			

Table 2. Data from the Office for National Statistics expressing actual deaths in care homes attributed to COVID-19 and non-COVID, with 2019 deaths as a comparator[22]

are imprisoned.[23] Lack of supervision and social contact increases the risk of falls and leads to depression, one consequence of which is a refusal to eat. Relatives and friends are unable to help by encouraging them with their meals. Those who are free to roam in a care home will not understand the need for social distancing and the wearing of a mask.

Care home managers were coerced by government policy to take pressure off precious hospital beds, by accepting hundreds of patients with unknown COVID-19 status, since the need to test every patient, whether or not symptomatic, was only introduced in mid-April.[24] At the same time, managers were struggling to acquire personal protective equipment (PPE) for their homes.[25,26] Once in a home, the virus could spread rapidly and in some cases the mortality rate exceeded 10%.[1] Some care home managers, faced with the loss of income following deaths, felt pressurised to fill the vacant beds, putting even more people at risk. There remains an acrimonious debate between journalists and NHS England about denying frail older people potentially life-saving care at the height of the pandemic.[27]

A large number of care homes avoided COVID-19 completely. These pre-empted the government lockdown by banning all visitors and refusing to admit any new residents, unless they had tested negative for the virus. This disciplined approach preserved their patients, and their income. In one Doncaster care home, all staff lived in the home from the start of lockdown and thus ensured the safety of their 21 vulnerable residents.

The meaning of triple jeopardy

The triple jeopardy of our title is a response to COVID-19.[2] The original concept of triple jeopardy appeared in the 19th century when female anti-slavery campaigners realised that they would only be truly free when emancipation was combined with female equality and social justice.[28] It is interesting to apply the original elements of triple jeopardy (gender, social class and race) to the 21st century predicament of COVID-19. The Goldacre team[29] examined the influence of these factors using cross-sectional data on 16,749 patients hospitalised for COVID-19. For reasons that are not clear, men have a significantly higher death rate than women, with a hazard ratio of 1.59 (1.53–1.65). There was a consistent pattern of increasing risk with greater deprivation, with the most deprived quintile having a hazard ratio of 1.79 compared to the least deprived. Very little of this increased risk was explained by pre-existing disease or clinical factors, suggesting that other social factors have an important role.

Compared with people of white ethnicity, black and South Asian people are at higher risk, even after adjustment for other factors: HR 1.48 (1.29–1.69) and 1.45 (1.32–1.58), respectively. Only a small part of the excess risk was explained by a higher prevalence of medical problems such as cardiovascular disease or diabetes among BAME people, or by higher levels of deprivation. A full independent government enquiry into the disproportionate COVID risk in ethnic minority groups has been called for in parliament.[30] So the original triple jeopardy factors, gender, social equality and race, remain relevant to this day and raise questions for the government and for society.

The future

COVID-19 has not gone away and a second wave is now upon us. Initially, the rising number of infections in the second wave was not accompanied by an increase in hospital admissions or mortality, probably because younger people were infected. More recently, admissions have increased among older people and mortality rates are rising. The triple jeopardy of diabetes, age and frailty remains a risk and we need to focus on the factors we can influence – diabetes control, obesity (a long-term project) and improved procedures in care homes, particularly for people with diabetes.

The delivery of diabetes care has changed irrevocably during the COVID-19 crisis and the onus is now on diabetes teams to ensure that people can access the care they need, be it face to face or virtual, in primary or specialist care. With the demise of Public Health England the future of an obesity strategy is uncertain, but at least the Prime Minister is a convert to the cause.[31]

It goes without saying that NHS policies for discharging people from hospital to residential care need to be revised to avoid a repeat of the spring catastrophe. Guidance for diabetes management in care homes has been issued by the Joint British Diabetes Societies[32] but the underlying problem of staff shortages and

consequent lack of experience of diabetes management is difficult to address. Some areas have improved diabetes care for residents by transferring the responsibility of glucose monitoring and insulin administration from district nurses to care home workers. This allows timely administration of insulin and avoids the need for nurses to travel from home to home, taking the virus with them as they go. However, to be successful it requires staff education and a stable workforce.

Conclusion

All governments have been tested by the pandemic and some, though by no means all, have been found wanting. In the UK the COVID-19 pandemic has shone a light on the chasm between the haves and the have-nots in society. People included in both the original and the new COVID definition of triple jeopardy have fared badly, with those living and working in care homes identified as one of the most marginalised groups in our society. Now the second wave is upon us, it is disappointing that we appear to have learned little from the mistakes of the first and the concept of 'triple jeopardy' remains just as important in identifying and protecting those at most risk.

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Declaration of interests

There are no conflicts of interest declared.

KEY POINTS

- In the context of COVID-19, triple jeopardy is defined as those who are older, are frail and have diabetes. People in this group have suffered the highest mortality from the virus
- People with diabetes in all age groups have a higher mortality rate from COVID, but age and frailty dominate the risk of dying
- In the first three months of the crisis nearly 40% of all COVID deaths in England were in care home residents, many of whom may have had diabetes. Thus people in care homes became a new marginalised group
- As the second wave of COVID gathers pace, care homes must be given greater priority for frequent testing of both residents and staff, as well as the provision of full personal protective equipment

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